Abstracts Posters Andrade first author 1969-2010

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Conditions necessary for the existence of pervasive damping are established for the specialized configuration. The stability of the second order, constant coefficient linear differential equations of motion is examined using a corollary of the Thomson-Tait-Chetaev theorem.

Davidon's variable metric algorithm modified for problems in parameter optimization involving constraints is employed to select configuration parameters to minimize a quadratic cost functional involving deviation angles and their rates from an equilibrium orientation in circular orbit. The parameters considered are the moments of inertia of the control body, the moment of inertia about the main body yaw axis, the orientation of the relative angular momentum vector in one of two specified planes, the "rotor strength," the spring and the damping constants. The dependence of the final parameter values achieved upon the initial conditions assumed and the relative weighting assumed in the quadratic cost functional is specifically noted. A mathematical basis is established to facilitate the establishment of those initial conditions that will provide an upper and lower bound upon the transient response achievable as well. A basis for design of a satellite is also established in the event that a statistical description of the initial conditions to be experienced is available.

M $3.00; X $9.25. 201 pages.

AN ARC-HEATED Ar-He BINARY SUPERSONIC MOLECULAR BEAM WITH ENERGIES UP TO 21 eV.

(Order No. 70-2280)

Wen-Shean Young, Ph.D.
University of California, Los Angeles, 1969

Chairman: Professor Eldon L. Knuth

A molecular-beam apparatus combining the aerodynamic acceleration and arc-heating techniques has been developed. Semiempirical equations which predict the beam density and the beam energy have been derived. An energy of 21 eV and a density of 4×10^9 molecules/cm^3 have been experimentally observed for argon accelerated by helium.

The phenomenon of species separation associated with (a) expansions of a binary-mixture in a free jet and (b) thermal diffusions due to arc-heating is also investigated.

To facilitate the experimental studies, a magnetoplasmadynamic arc-heater has been developed.

To eliminate some of the deficiencies of a conventional single-disk time-of-flight (TOF) chopper, a novel dual-disk TOF chopper has been introduced. Analytical expressions relating the dual-disk TOF signals to the density and the pertinent parameters of the speed distribution function of the beam have been derived. It is demonstrated that use of this new chopper simplifies greatly the experimental and data-reduction procedures.

This study reveals also that the application of the conventional TOF technique introduces a serious uncertainty in the measurement of the speed ratio of a high-speed molecular beam. The solution of this problem requires new concepts in beam-modulation techniques.

M $3.00; X $7.00. 149 pages.

ENGINEERING, BIOMEDICAL

COAGULATION-RESISTANT SURFACES AND A MECHANISTIC MODEL OF ADSORPTION ON POLYMER SURFACES.

(Order No. 70-1922)

Joseph D. Andrade, Jr., Ph.D.
University of Denver, 1969

The blood/materials interface is a crucial factor in the successful use of solid materials for blood-contact applications. The interactions which occur at such interfaces will not be understood until one thoroughly understands the mechanism of adsorption from aqueous solution, particularly onto polymer surfaces.

A mechanistic model of adsorption of apolar molecules from aqueous solution onto apolar polymer surfaces is presented. The nature of adsorption, the structure of water, and the forces which exist between molecules are all considered. The model shows that adsorption is a natural consequence of the asymmetric force field which exists in the vicinity of an interface. It shows that solvent-solvent and solvent-solute interactions are of particular importance, especially in aqueous systems. The solvent content of the adsorbate is considered, resulting in the conclusion that adsorption will not tend to occur on a solvent-loaded surface. The model predicts and provides a mechanistic explanation for monolayer and multilayer adsorption; it also discusses and predicts the orientations of adsorbed species. The role of polymer crystallinity effects and "active sites" is briefly examined; however, the role of the solid surface is shown to be minor with respect to solvent-solvent and solvent-solute effects. Calculations are presented for a $-CH_2-$ group, ethane, butane, and hexane. Qualitative discussions are given for the adsorption of polar molecules and macromolecules, notably proteins. The structure of ribonuclease is examined; it is shown that different areas on the protein will have significantly different intermolecular interactions with the surrounding solvent or with a nearby adsorbate. The conclusion is that a protein must be expected to adsorb by different mechanisms on different surfaces. The surface-protein interactions may be highly dependent on the orientation of the protein with respect to the solid surface. The adsorption of albumin, gamma globulins, and fibrinogen is also discussed. The model and its predictions are compared with available experimental data.

The rationale for the preparation of potentially enzyme inhibitory and non-thrombogenic/polymers, the polyorganofluorophosphates, is briefly discussed. The rationale for preparing proteinated surfaces is also analyzed; the preparation of albuminated polystyrene is treated in detail and its non-thrombogenic behavior is discussed. A brief mention is given to the potential use of fluorescence microscopy as a tool for studying protein adsorption on the microscopic level.

M $3.00; X $8.40. 183 pages.

THE DIELECTRIC PROPERTIES OF STRUCTURED WATER

(Order No. 70-2884)

George Takashi Koide, Ph.D.
The University of Rochester, 1969

Dielectric measurements on protein solutions (Schwan, 1957, 1965; Grant, 1965; Arron, 1966; Pennock, 1967) show a dispersion in the v.h.f.-u.h.f. region. It has been postulated

Soc. Plastics Engrs, 34th Ann. Tech Conf. 4/76

HYDROGELS FOR MEDICAL AND RELATED APPLICATIONS

Joseph D. Andrade
Department of Materials Science and Engineering
and Institute for Biomedical Engineering
University of Utah
Salt Lake City, Utah 84112

INTRODUCTION

There is considerable interest and activity in the application of synthetic and biological polymers in medicine. Synthetic polymers are widely used as surgical and dental implants as well as for blood bags, syringes, tubing, etc. Most of the materials used in medicine have properties greatly different from the tissue with which they are interfaced or replacing.

Excepting bones, nails, and the outer layers of skin, mammalian tissues are highly aqueous materials, with water contents ranging up to 90% (blood plasma).

Hydrogels are three dimensional networks of hydrophilic polymers, generally covalently or ionically cross-linked, which interact with aqueous solutions by swelling to some equilibrium value. Aqueous gel networks can be relatively strong (such as in cellulose dialysis membranes) or relatively weak, generally becoming weaker as the water content increases, though such variables as the nature of the cross-linker, polymer network, tacticity, and crystallinity can significantly influence the mechanical behavior.

Interest has focused on the utilization of the bulk or the surface properties of hydrogels for biomedical applications (3). Because of this growing interest, a Symposium on Hydrogels for Medical and Related Applications was organized under the auspices of the Polymer Division of the American Chemical Society. The Symposium was held August 27-28 at the Chicago Meeting of the ACS. Preprints of the papers are available (1). Many of the papers presented are included in a Symposium volume which is in press (2).

BULK PROPERTIES

Bulk properties of interest include swelling particularly dimensional changes upon swelling or deswelling (4). This is of particular interest in "swelling implants" (5), implants which can be implanted in a small dehydrated state via a small incision and then swell to fill a body cavity and/or to exert a controlled pressure. The swelling of synthetic and natural gels may also help elucidate swelling and osmotic mechanisms in biological tissues (4, 6-7).

A related bulk property is the permeability of hydrogels for low molecular weight solutes. Solute diffusivity in gels is of particular interest in sustained drug release applications (7,8) and in the transport of solutes to gel-entrapped macromolecules, particularly enzymes immobilized in the gel network (9). Ion interactions or partitioning within the gels are important in bone interfacing applications (10).

The Symposium brought together a number of fairly basic studies of gel networks and a number of practical applications based on network properties (1,2).

Aqueous gels are relatively subtle systems which equilibrate with and "follow" many environmental changes. The properties of such gels can be highly dependent on cross-linker levels, impurity levels of comonomers, catalyst residues, and stereoregularity. These variables were discussed for hydrophilic methacrylate ester monomers and their gels, the most discussed systems at the meeting. Monomer analysis and purification (11,12), free radical initiator effects (13), and tacticity (14) were discussed for the poly(hydroxyethyl methacrylate) system.

The bulk properties of synthetic hydrogels can be widely varied and perhaps tailored to specific end uses. Though the poly(hydroxyethyl methacrylate) system is the most widely studied for medical applications, a large repertoire of gel types are available and have been applied to varying degrees in medicine (3). Questions of long term biostability or intentional biodegradeability are also very important, but were not discussed at the Symposium.

SURFACE PROPERTIES

The surface and interfacial properties of hydrogels are somewhat similar to those of natural biological gels and tissues. A number of analogies or comparisons have been made between the hydrogel/water interface and the living cell/physiologic solution interface (15). Such interfaces are difficult to study and interpret as many of the assumptions of classical surface chemistry break down (16,17). The effect of the gel/water interface on interfacial fluid dynamics was briefly discussed (16). The use of neutral gel coatings to reduce local fluid movement (electroosmosis) in particle electrophoresis experiments was discussed by two groups (18,19). It was shown that the interface electrokinetic potential (as measured by the streaming potential) can be varied by use of appropriate comonomer compositions (19), though some caution was urged in the interpretation of electrokinetic measurements of gel/water interfaces (17).

The wettability of hydrogel surfaces was discussed (20) and shown to be rather complicated, perhaps depending on the mobility of polymer segments in the interfacial zone. Protein adsorption at certain gel interfaces was also discussed and related to interfacial free energy arguments (21).

Aqueous gel surfaces are of interest for use in blood-contact applications, as tubing, catheters, and vascular devices (3,22). Such applications are dependent on the nature of the gel/blood interface. As hydrogels generally lack suitable mechanical properties for vascular device applications, there has been considerable activity in coating or grafting the gels to mechanically suitable supports (3). Several papers discussed the grafting of gels to various supports (23-25).

A number of papers discussed platelet interactions with aqueous gels (see Reference 1) and several discussed general blood compatibility (3,22). One paper considered the application of hydrogels as a substrate for in vitro cell or tissue culture studies (26). Considerable data on the blood compatibility of hydrogels is available, particularly for polyacrylamide (27), and there is considerable interest and activity among medical research scientists and a number of commercial firms in hydrogel-coated catheters, drains, and other conduits. The use of gels as substrates for in vitro cell or tissue culture is also of interest (26,28).

CONCLUSIONS

Aqueous gel networks have an important role to play in biomedicine, not only as inert blood conduits and devices, but as biochemically and pharmaceutically active elements as well. The role of ion and solute partitioning or interactions with gels will prove important for such applications as enzyme entrapment, sustained drug or ion release, bone induction or calcification, as well as for the more popular applications of blood and tissue interfacing. Suitably equilibrated and solute "stocked" gels should prove very important for cell and tissue culture applications.

Control of hydration/dehydration phenomena, particularly

hysteresis effects, is needed in order to be able to ship and store hydrogel products dry to reduce bulk and the possibility of microorganism contamination.

This Symposium brought a number of basic and applied researchers together, exploiting the unique bulk and interfacial properties of gels. It was clear, however, that we will hear a good deal more in the near future about synthetic hydrogels.

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TALK Abstract 1980

University of Wisconsin Madison

CENTER FOR HEALTH SCIENCES
School of Pharmacy
Office of the Dean
425 North Charter Street
Madison, Wisconsin 53706
Telephone: 608/262-1414

October 15, 1979

Dr. Joseph Andrade
Department of Bioengineering
Merrell Engineering Building
University of Utah
Salt Lake City, Utah 84112

Dear Joe:

Thanks for agreeing to be part of our symposium on solids. I'm really looking forward to seeing it all come together. Could I ask you to submit a brief biographical sketch at the time you send in the abstract. We will cover your expenses as I described in my letter.

My plans for fall semester of 1980 are still up in the air, but I'll let you know if I can arrange to spend some time with you. If I did, it would be for one or two months at most, but it should give me some time to think before I resume full academic duties.

Best personal wishes.

Sincerely,

George

George Zografi
Dean and Professor

GZ:bh

Other topics and speakers: Characterization of Hydrophilic Colloidal Solid Surfaces, Prof. J. White, Purdue University, Department of Agronomy

Characterization of Porous Solid Surfaces, Prof. J. T. Carstensen, University of Wisconsin

ABSTRACT

Characterization of Polymer and Related Organic Solid Surfaces

by

J.D. Andrade and R.N. King
Departments of Bioengineering,
Materials Science and Engineering, and Pharmaceutics and
Surface Analysis Laboratory
University of Utah
Salt Lake City, Utah 84112

The characterization of organic polymer surfaces and other solid organic materials is of considerable interest in a variety of pharmaceutical and related applications. The surface properties of container materials are important in predicting and controlling adsorption processes of active agents. The interaction of polymers and polymer networks with drugs is of interest and practical application in the area of sustained and controlled drug delivery devices. The surface properties of pressed materials, such as pellets and tablets, are, of course, very important in the overall swelling and pharmaceutic aspects of these materials.

X-ray photoelectron spectroscopy (XPS), commonly called ESCA (electron spectroscopy for chemical applications), is perhaps the most powerful tool available today for the routine, straightforward, unambiguous characterization of organic surfaces. Although the instrument is relatively expensive, the sample throughput and data interpretation with this technique is rapid and straightforward. XPS analysis is now available from a number of commercial labs at reasonable rates. Basically the technique provides a total elemental analysis, with the exception of hydrogen and helium, of approximately the top 50 angstroms of any solid organic material which is vacuum stable or can be made vacuum stable by cooling to low temperatures. Although the technique cannot be considered a trace technique in that atomic ratios of one part in 1,000 or less are difficult to detect, its exquisite surface sensitivity makes it possible to obtain full spectra from a volume of 1 x 5 mm by 50 angstroms or a total sample size of approximately of 0.25 nanograms. This makes the technique very helpful for the bulk and routine elemental analysis of extremely small quantities of materials. The surface chemistry of container and packaging materials is very easy to characterize with such a technique. Low degrees of surface oxidation, the presence of small quantities of mold release agents, surface active agents, antistatic agents, adsorbed films, and related questions can be readily answered by the technique. The general principles of XPS, including instrumentation, sample preparation, and data analysis, will be discussed and appropriate examples from the biomaterials area will be given.

Contact angle methods are highly useful for determining the surface and interface energetics of organic solid materials. These energetics are of importance in attempting to deduce the polar and apolar components of the surface and are, of course, related to such questions as swelling,

solubility, and adsorptive characteristics. The contact angle method discussed emphasizes characterization of the organic solid-water or aqueous solution interface. For a variety of reasons, the surface energetics of the solid-water interface are often very different from that deduced from a study of the solid-air interface, due to the tendency of the solid material to re-equilibrate and appropriately re-orient with a surrounding phase. This is particularly important in hydrophilic solid materials, including hydrogels, which may orient and equilibrate in an aqueous phase such as to minimize their interfacial free energy but will tend to orient or equilibrate with an air phase so as to minimize their surface free energy. The contact angle technique consists of applying air bubbles or octane droplets directly to the solid water interface. The appropriate equations, assumptions, and theoretical treatment of the data will be presented and examples will be given from the literature, primarily in the area of methacrylate-based hydrophobic and hydrophilic materials of interest for controlled drug release applications.

The third surface parameter of interest is that of interface potential or surface charge. The technique commonly used to measure surface potential of particles is their electrophoretic mobility. This is not applicable to low surface area solid materials such as flat sheets and films. A related technique, streaming potential, is therefore used. A flat plate streaming potential apparatus will be described and data presented on a variety of synthetic polymers with varying degrees of fixed negative and fixed positive charges. These materials are being studied as cell culture substrates to consider the effect of substrate surface charge on the behavior of cells in in vitro cell culture.

Methods of surface modification of polymer materials for specific applications will also be described, primarily radio frequency glow discharge induced oxidation of polymer surfaces to increase wetability and adhesion.

The question of surface structure and morphology will be addressed briefly and the technique of scanning electron microscopy in the back-scattered electron detection mode will be discussed and results presented using polymer blends of various surface and bulk structure.

The talk will conclude with a very brief mention of several recently developed techniques which have high potential for the study and characterization of organic solid surfaces, including secondary ion mass spectroscopy, (SIMS) and the laser Raman microprobe.

Reserv at Sheraton for Tues & Wed nites

ACADEMY OF PHARMACEUTICAL SCIENCES

A Subdivision of the American Pharmaceutical Association for Member Scientists in Research, Teaching, Production and Marketing

December 6, 1979

Reprint file

Andrade — ?

APhA - 4/80

Professor Joseph Andrade
College of Pharmacy
University of Utah
Salt Lake City, UT 84122

Dear Professor Andrade:

We are pleased to learn from our program chairman that you will participate in a symposium entitled, "Properties of Solid Surfaces." As you know, this symposium will be sponsored by the American Pharmaceutical Association Academy of Pharmaceutical Sciences during the 127th Annual Meeting of the Association, ~~April 19-24, 1980 in Washington, D. C.~~ Your symposium, which will be held on Wednesday, April 23, 8:30 a.m.-11:30 a.m. in the Richmond and Arlington Suites of the Sheraton Washington Hotel, is sponsored by the ~~APS Sections on Basic Pharmaceutics~~ and Pharmacology and Toxicology.

The Academy will publish abstracts of all papers presented during the meeting before the six APS Sections. We understand from your program coordinator, Dr. George Zografi, that you will submit your abstract and biographical sketch forms to him. Dr. Zografi will forward your forms to this office. As a program participant, you will receive a complimentary copy of the abstracts book prior to the meeting.

Please let us know, as soon as possible, if there is any audiovisual equipment you will require for your presentation. We must have final audiovisual equipment requirements by no later than February 14, 1980.

Enclosed for your convenience is a copy of the hotel reservation form for the 1980 APhA Annual Meeting. If the Academy of Pharmaceutical Sciences staff can be of any assistance to you in preparation for your presentation during the 1980 APhA Annual Meeting, please do not hesitate to contact us.

Sincerely,

Connie Johnson Tyler

Constance Johnson Tyler
Special Assistant for
Subdivision Activities

Enclosures
cc: Dr. Sylvan G. Frank, Basic Program Chairman
Dr. Kenneth R. Heimlich, IPT Program Chairman
Dr. George Zografi, Program Coordinator
Mr. Ronald L. Williams, Executive Secretary

Dear Ms Tyler

2215 CONSTITUTION AVENUE, N.W., WASHINGTON, D.C. 20037 • (202)628-4410

University of Wisconsin Madison

CENTER FOR HEALTH SCIENCES
School of Pharmacy
Office of the Dean
425 North Charter Street
Madison, Wisconsin 53706
Telephone: 608/262-1414

April 30, 1980

Dr. Joseph Andrade
Department of Bioengineering
University of Utah
Salt Lake City, Utah

Dear Joe:

Many, many thanks for an excellent presentation at our symposium in Washington. You did a superb job of pulling so much interesting material together! I'm sorry you had to rush away, but it was just so stimulating to spend even a few minutes talking science. I hope I can visit with you in the near future. There is so much you are doing which interests me.

I hope all financial arrangements are taken care of with the Academy. Please let me know if you have any problems.

Best personal wishes.

Sincerely yours,

George

George Zografi

GZ:bh

P.S. Did you happen to pick up the two slides I showed before your talk? If not, don't bother answering.

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1984 PRAGUE MEETINGS ON macromolecules

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Polymers in Medicine and Biology

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L10 EFFECTS OF PLASMA PROTEIN ADSORPTION ON PROTEIN CONFORMATION AND ACTIVITY

J.D. ANDRADE, V.L. HLADY, & R.A. VAN WAGENEN

Department of Bioengineering, University of Utah, Salt Lake City, Utah 84112, USA

ABSTRACT - Protein adsorption at solid-liquid interfaces may lead to significant changes in conformation. Such effects can be monitored *in situ* for native, unlabelled proteins using the total internal reflection spectroscopy method, by monitoring the UV fluorescence of tryptophan side chains at 320-350 nm. Such studies suggest a partial denaturation of human plasma fibronectin on hydrophobic silica and a blue shift for bovine albumin on hydrophilic silica.

CONFORMATIONAL DYNAMICS

Protein folding and denaturation studies show that the normal or native state is only marginally stable. The free energy change involved in the transition to a denatured state is only 5 to 14 kcal/mole--an energy corresponding to only a few hydrogen bonds per molecule! Adsorption-free energies of proteins are normally in the range of 5 to 20 kcal/mole, thus adsorption-induced "denaturation" is highly probable. Proteins in an altered micro-environment, such as adjacent to or on a solid surface, must be expected to be conformationally different from like proteins in the bulk solution.

ADSORPTION & CONFORMATION

Many studies of proteins at air-solution interfaces have indirectly established that the adsorbed proteins undergo detectable conformational changes. Similar studies at solid-liquid interfaces are few.

Total internal reflection fluorescence (TIRF) spectroscopy has recently been applied by several groups and complete reviews are now available. The method can easily follow the kinetics of adsorption using proteins labelled with extrinsic fluors, such as fluoroscein or rhodamine. The intrinsic UV fluorescence of tryptophan (Trp) can be used to follow adsorption. The UV approach has the advantage that the tryptophan fluorescence is sensitive to the local micro-environment and no label is required. The major disadvantage of the UV method is the UV photochemical changes which occur, although such changes can be minimized by working at low radiation dose levels.

The intrinsic UV fluorescence of proteins is dominated by the tryptophan indole rings. The absorption maximum is 280-290 nm with the fluorescence maximum ranging from 315-355 nm, depending on the local environment of the indole side chains. Quantum yields range from 0.04 to 0.50; 0.10 is a common value. As the local environment polarity or dielectric constant increases, the maximum shifts up to 355 nm, such as for an indole ring in water or buffer. Trp moieties in highly hydrophobic environments fluoresce at 315-320 nm. Thus the fluorescence emission maximum (and the quantum yield) provide indirect information as to the local environment of the Trp fluors.

Although a number of proteins of interest (human serum albumin, for example) contain a single Trp, most contain two or more. Thus the spectrum observed is the sum of all active Trp fluors, making it

difficult to deduce the local environment of each fluor. Nevertheless, the UV fluorescence emission spectrum is useful in deducing orientation and/or conformation changes upon adsorption.

MATERIALS & METHODS

Intrinsic UV TIRF was used; the apparatus has been described. Care was taken to minimize UV photodegradation by blocking the beam except during the actual measurements and by using continuous rather than pulsed UV sources.

RESULTS & DISCUSSION

Fibronectin adsorption in the static mode from 0.05 mg/ml showed very different kinetics for the hydrophobic and hydrophilic surfaces. The data for static and flow adsorption and desorption have been reported. The quantity of interest here is the fluorescence maximum, which for Fn on hydrophilic silica is identical to that in bulk solution, suggesting no major conformational change upon adsorption (Table 1).

TABLE 1 Fluorescence maximum of Fn in different environments

Environment	Fluorescence Maximum, nm
Bulk-PBS buffer	321
Bulk-PBS/8M urea	330
Bulk-PBS/3M guanidine Cl	350
Adsorbed on hydrophobic silica	326
Adsorbed on hydrophilic silica	321

The Fn-surface interactions probably involve the charged groups on the surface of the molecule, most likely the highly positively charged heparin binding regions of the molecule (pK=8-9).

Fn adsorbed on hydrophobic silica, however, fluoresces at 326, suggesting a slight denaturation of the molecule. Fn interactions with the hydrophobic surface may involve some of the apolar residues in the protein interior, suggesting a partial denaturation.

Bovine albumin has been studied only on hydrophilic quartz to date. The fluorescence maximum (1 mg/ml BSA in PBS) is 342nm and shifts to 333 nm upon adsorption. These results suggest that the adsorption of BSA on to silica changes the conformation of the molecule such that the two Trp fluors are in a more hydrophobic environment.

CONCLUSIONS

We report that human plasma fibronectin adsorbed on hydrophobic and hydrophilic quartz shows maxima of 326 and 321 nm, respectively, suggesting that Fn adsorption on the hydrophobic quartz results in some conformation change of the adsorbed protein. Bovine serum albumin shows a 9 nm blue shift (from 342 nm in solution to 333 nm in the adsorbed state) upon adsorption onto hydrophilic quartz, suggesting a more hydrophobic environment for the Trp as a result of the adsorption process.

These preliminary studies demonstrate that intrinsic TIRF can be used to deduce micro-environmental and possibly conformation changes in adsorbed proteins.

S1 LIPOSOMES WITH PHARMACOLOGICALLY ACTIVE HEAD GROUPS

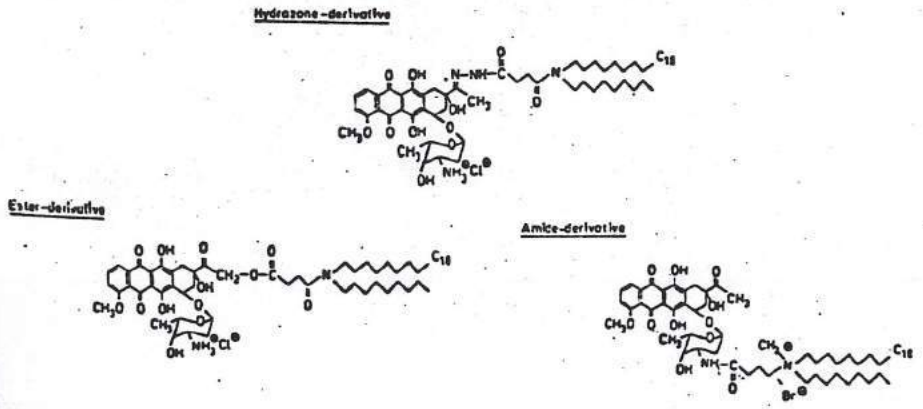
M.EMMELIUS, H.RINGSDORF and B.SCHMIDT

Institute of Organic Chemistry, University of Mainz, FRG

Summary

In the last years different polymeric carrier systems for pharmacologically active substances have been discussed. Beside random coils micell-forming polymers and liposomes have been investigated. As described previously, the amphiphiles of liposomes (e.g. phospholipids) show a number of different interactions with biological molecules such as adsorption on lipoproteins, lipid exchange with cell-membranes, fusion and endocytosis. For this reason liposomes filled with drugs have been reported as carrier systems. A new concept deals with liposomes prepared from lipids, where the drug is fixed itself as polar head group. A drug containing the structural components of membrane forming phospholipids should result in similiar properties under biological conditions. On this base anthracycline derivatives containing two long alkyl chains and a hydrophilic head group have been synthesized. Three types of covalent linkages between drug and hydrophobic moity have been studied: hydrazone, ester and amide. These linkages may be cleaved under hydrolytic or enzymatic conditions.

LIPOPHILIC DERIVATIVES OF ANTHRACYCLINES



Ab-ANDR-2

THE HEMOGLOBIN HYPOTHESIS: HEMOGLOBIN AND HAPTOGLOBIN SURFACE PROPERTIES

J. Andrade, J. Chen, J. Pierce, R. Lowe, D. E. Gregonis

Department of Bioengineering, University of Utah, Salt Lake City, Utah 84112

INTRODUCTION: The hemoglobin (Hb) hypothesis is based on five somewhat circumstantial pieces of evidence:

1. Horbett has reported [1] that Hb readily adsorbs on apolar surfaces, totally out of proportion to its solution concentration. Surface enhancements range 10 to 100 fold that of other plasma proteins.
2. The Battelle biological infrared spectroscopy group commonly observe IR bands in in vivo adsorption experiments which may be related to Hb.
3. Pierce and Andrade [3] have studied the adsorption of various ligand forms of Hb on partially hydrophobic alkyl agarose substrates and found that the adsorption of Hb is dependent on the ligand state of the molecule.
4. Coleman and others in the Artificial Heart Group at Utah observed significant surface discoloration in retrieved artificial heart implants which appeared to correlate with regions of turbulance and perhaps local hemolysis and with actual pumping diaphragm abrasion resulting in local hemolysis [4]. They suggest that the coloration may be due to heme byproducts.
5. It is generally accepted that implants in the arterial and venous systems behave differently perhaps due to pO_2 pH, pressure, and/or flow differences, but perhaps also due to different ligand forms of the Hb which may be present.

It is clear that blood contact with foreign surfaces, even under mild flow conditions results in local hemolysis, in large part dependent on specific surface interactions [5]. Thus Hb may be present in sufficient concentration at local regions where sublethal hemolysis occurs, even though the systemic concentration of the protein may be very low.

Figure 1 summarizes the various forms of hemoglobin. OxyHb when released into the plasma, is rapidly and irreversibly bound by haptoglobin (Hp), a plasma-glycoprotein [6].

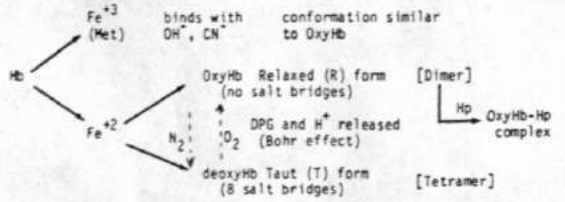


Figure. Different forms and characteristics of Hb. Oxy and deoxy Fe^{+2} are the forms of major clinical interest.

The hemoglobin hypothesis is formulated as follows: If there exists regions of local turbulence or other trauma which can result in local Hb release, that released Hb can adsorb onto foreign surfaces in concentrations orders of magnitude greater than one would expect based on the solution concentration. Hb released on the venous side (in the deoxy form) may adsorb significantly differently than Hb released on the arterial side (in the oxy form and complexed with Hp). This behavior, if it occurs in vivo, may be in part responsible for the different blood compatibility of implants in the venous and arterial system.

If surfaces containing Oxy or deoxyHb, Hp or the Oxy Hb-Hp complex prove to show different blood interactions, then surfaces designed for arterial compatibility may require different properties than those destined for venous application. It may also be that in a complex cardiovascular device where there are regions of local blood turbulence, the surface properties in local regions of blood trauma may even need to be different than the surface properties in other regions of the device.

Results: To date we have only studied the adsorption of pure human Oxy and deoxyHb and, in a preliminary day, human Hp (type 2-2). Details on protein and surface preparation and experimental methods are available (7).

The 60 minute static adsorption data for 0.25 mg/mℓ pure Hb solutions are given in the table, together with the receding water contact angles as determined by the Wilhelmy plate technique (8), for 5 different surfaces. Note that the adsorbed amounts range from ~ 0.1 to 0.6 Mg/cm^2 for Oxy Hb and from 0.3 to 0.8 Mg/cm^2 for deoxy Hb. There is a strong correlation between the adsorbed amounts and the receding water contact angle. The advancing angle does not correlate very well. This is expected as the receding angle is more representative of the interfacial state in aqueous solutions.

Preliminary studies of human Hp adsorption by the total internal reflection intrinsic fluorescence (TIRF) method (9) on both clean (hydrophilic) and silanized (hydrophobic) quartz indiate substantial adsorption which is largely irreversible upon solution dilution. Although Hb adsorption has not been detected by intrinsic UV TIRF due to its very low quantum efficiency (10), Hp is readily detected.

Discussion/Conclusions: Although this work is ongoing, the following preliminary conclusions can be drawn (7):

1. DeoxyHb adsorbs more than Oxy Hb on all surfaces examined (Table). The deoxyHb surface is more hydrophobic than the Oxy form, due to the conformational change upon oxygenation. The increased adsorption of deoxyHb on hydrophobic surfaces may be due to a surface-induced dimerization (7), which would make the Oxy Hb dimer more hydrophobic than the deoxy tetramer.
2. The more hydrophobic the surface, the more adsorption of both Hb forms.

Table: Hb Adsorbed ($\mu g/cm^2$) at 60 minutes of exposure to a 0.25 mg/ml H^3-Hb in PBS, pH 7.4, 20°C. (std. dev. ~ : 0.1 $\mu g/cm^2$). θ_{rec} is the receding water contact angle. θ_{adv} is the advancing water contact angle.

Material →	Glass	Polyether Urethane	NPS Glass	Poly-styrene	PDM SO
θ_{rec} θ_{adv}	2 ± 5° 15 ± 5°	30 ± 10° 75 ± 10°	62 ± 10° 75 ± 10°	70 ± 5° 88 ± 5°	75 ± 5° 110 ± 5°
OxyHb	0.21	0.14	0.36	0.56	0.58
deOxyHb	0.37	0.31	0.47	0.72	0.80

References available from senior author.

I 4

PROBING POLYMER SURFACE DYNAMICS BY CONTACT ANGLE HYSTERESIS AND ESCA

by

J. D. Andrade and W-Y Chen
College of Engineering
University of Utah
Salt Lake City, Utah 84112, USA

Polymeric materials generally exhibit various molecular motions and relaxations. Such relaxation processes, which include the glass transition temperature, have significant effects on physical and mechanical behavior. Polymer molecules and segments at surfaces and interfaces also exhibit motions and relaxations. In air or vacuum, such motions "permit" the surface to structure to minimize the surface free energy. In aqueous solution, the polymer surface structures and orients to optimally interact with the aqueous solvent, thereby minimizing the interfacial free energy. XPS and related high vacuum techniques probe the vacuum-equilibrated surface. The best way to probe the polymer-liquid interface is via dynamic contact angle or wetting methods. We describe the Wilhelmy Plate method for dynamic contact angle measurement, permitting both advancing and receding angles to be measured continuously. Case studies using various methacrylate copolymer and polyethylene oxide surfaces will be presented and discussed.

EUROPEAN CONFERENCE ON APPLICATIONS OF SURFACE AND INTERFACE ANALYSIS

ECASIA 85

EUROPEAN CONFERENCE ON APPLICATIONS OF SURFACE AND INTERFACE ANALYSIS

ABSTRACTS

14 - 18 October 1985
Veldhoven
THE NETHERLANDS

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FINAL PROGRAM

Joint Topical Workshop

on

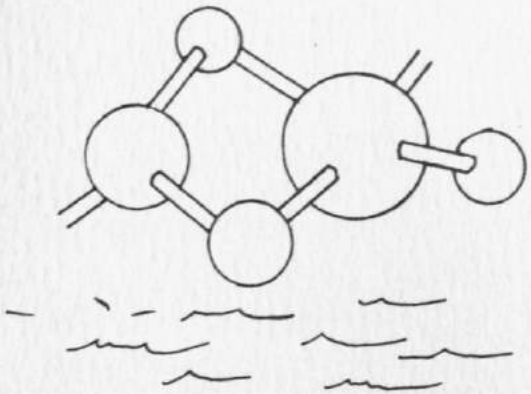
Water – Polymer Interactions

sponsored by

Division of Polymer Chemistry, Inc.
American Chemical Society

and

Academy of Pharmaceutical Sciences



March 12-15, 1986
Monterey, California

Co-Chairmen

L.G. Donaruma, Division of Polymer Chemistry, Inc.
G. Zentner, Academy of Pharmaceutical Sciences

FINAL PROGRAM

Water-Polymer Interactions

Wednesday, March 12, 1986

Registration – 3:00 p.m.-9:00 p.m.
Welcoming Reception – 6:30 p.m.-9:30 p.m.

Thursday morning – March 13, 1986

Presiding – L.G. Donaruma

8:15 a.m. Welcoming Remarks – **L.Z. Benet**
President, Academy of Pharmaceutical Sciences

8:30 a.m. **W.J. Bailey**
University of Maryland, College Park, Maryland
"Biodegradable Polymers"

9:15 a.m. Discussion

9:45 a.m. **A.S. Hoffman**
University of Washington, Seattle, Washington
"Selected Applications of Aqueous Polymer Separations in Biotechnology"

10:30 a.m. Discussion and Coffee Break

11:00 a.m. **I.R. Schmolka**
Grosse Ile, Michigan
"Aqueous Block Copolymer Surfactant Gels"

11:45 a.m. Discussion

12:15 p.m. Lunch – Afternoon free

Thursday evening – March 13, 1986

Presiding – A.R. Mlodozeniec

6:30 p.m. **F.J. Holly**
Texas Tech University, Lubbock, Texas
"The Hydrogel-Water Interface"

7:15 p.m. Discussion

7:45 p.m. **J.D. Andrade**
University of Utah, Salt Lake City, Utah
"Water-Induced Restructuring of Polymer Surfaces"

8:30 p.m. Discussion

9:00 p.m. **D.A. Tirrell**
University of Massachusetts, Amherst, Massachusetts
"Polymer Adsorption on Bilayered Membrane Surfaces"

9:45 p.m. Discussion

Friday Morning, March 14, 1986

Presiding – S.C. Israel

8:30 a.m. **A. Silberberg**
The Weizmann Institute, Rehovot, Israel
"Polymer Configuration as a Sensitive Indicator of the Solvent-Polymer Segment Interaction"

9:15 a.m. Discussion

9:45 a.m. **S.C. Temin**
MacroChem Corporation, Woburn, Massachusetts
"Polymer-Water Interactions in Hydrogels"

10:30 a.m. Discussion and Coffee Break

11:00 a.m. **U. Strauss**
Rutgers State University, New Brunswick, New Jersey
"Cooperative Effects in Coulombic and Hydrophobic Interactions Between Water and Polyelectrolytes"

11:45 a.m. Discussion

12:15 p.m. Lunch – Afternoon free

Friday evening – March 14, 1986

Presiding – G.M. Zentner and **L.G. Donaruma**

7:00 p.m. Banquet

H.A. Scheraga
Cornell University, Ithaca, New York
"Structure and Properties of Water in Aqueous Solutions"

Saturday morning – March 15, 1986

Presiding – G.M. Zentner

8:30 a.m. **H. Hopfenberg**
North Carolina State University, Raleigh, North Carolina
"Transport Phenomena of Small Molecules in Polymeric Materials"

9:15 a.m. Discussion

9:45 a.m. **S.W. Kim**
University of Utah, Salt Lake City, Utah
"Hydrogels – Swelling, Drug Loading Release"

10:30 a.m. Discussion and Coffee Break

11:00 a.m. **J. Kopecek**
Institute for Macromolecular Chemistry, Prague, Czechoslovakia
"Targetable Polymeric Drug Carriers: Influence of Polymer-Water Interactions on Biological Properties"

11:45 a.m. Discussion
Closing Remarks

The support of Merck Sharpe and Dohme Research Laboratories for this Workshop is greatly appreciated.

ACADEMY OF PHARMACEUTICAL SCIENCES
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July 29, 1985

RECEIVED
University of Utah
AUG 2 1985
Dean's Office
College of Engineering

Joseph D. Andrade, Dean
College of Engineering
University of Utah
2000 Merrill Engineering Bldg.
Salt Lake City, UT 84112

Dear Joe:

During March 12-15, 1986 the Division of Polymer Chemistry of the American Chemical Society and the Academy of Pharmaceutical Sciences will co-sponsor a workshop: "Polymer-Water Interactions." The workshop will be held in Monterey, California. As you may know, the workshop topic is one which is of great importance to both pharmaceutical and polymer scientists. We intend that this workshop will provide up-to-date information concerning advances and problems in the field.

We intend to provide a program in the format which has been so successful at the Gordon Research Conferences. That is to say, sessions in the morning and evening. Also, we shall have poster sessions during coffee intermissions and prior to evening sessions.

To the end of making this a most successful workshop, we are attempting to obtain the best possible speakers. Therefore, I am writing to ask if you would be willing to present a lecture at the workshop. It is anticipated that each lecture will be of 40 minutes duration with a 20 minute discussion period. We very much hope that you will accept this invitation. We are prepared to provide $400.00 toward your expenses and an additional $400.00 if the workshop attendance passes the financial break-even point by a sufficient margin.

As noted above, the theme of the workshop will be "Polymer-Water Interactions." We desire to address this theme through presentations which contain timely insights into water-polymer interactions in both the physical and chemical sense and which though basic or applied would be of interest to those in the pharmaceutical field as well as the

polymer field. Should you have any questions, or need additional information please do not hesitate to contact me. If you decide to accept our invitation, and we most heartily hope you will, we would be greatly obliged to receive from you a title for your presentation. I look forward to hearing from you at your early convenience.

Sincerely yours,

Gaylen

Gaylen M. Zentner, Ph.D.
Academy of Pharmaceutical Sciences

GMZ/pw

cc: L. Guy Donaruma
Division of Polymer Chemistry
American Chemical Society

Monterey Workshop 3/13/86

Water-Induced Restructuring of Polymer Surfaces

(1)

how do polymer surfaces interact w/ biol solns & tissues?

H_2O – 55M plasma ~ 90 wt%

ions ~ 1%

protein ~ 6–8%

other ~ 1%

(2)

Prot at A-F

Protein Adsorption — Ads'n

(3)

Why?

~~Stds~~ 2-DE-P.

(4)

Who?

Slides — Variables — Prot Surf] I-F
Prot Struct Media] I-F
Surface]

Prot XPAR

Time-Conform △

Now ignore protein & details of media → focus on solid surface.

Surf. Chem — classical assumptions:

Assump XPAR.

- Smooth —
- Homogeneous —
- Rigid
- Stable

Comes from Metal surfs

- No Interact — a Surf. Interact. Only.

A/W I-F rest of mat'l a "solid"

Poly-Gel interface — immob. liquid !

Silborberg — " " " a immob chain

Bulk Polymers — hierarchical structures

relax t & motions

1. homopolymer PMMA / PBMSO

T_g / T_β / . . . / T_{cryst}

t–T dependence / freq. dependence

2. copolymers
3. block copolymer
4. blends

↓ ↑ phase sep'n

polymers are generally incompatible —
can characterize in bulk —
solvent effects / good solv — poor solvent
anneal ⟹ equilibrium
particular morphology metastable —
kinetic constraints to equilib.
∴ polymers relax — have motions — etc...

<u>Surface?</u>

Well known polymers orient/order at A/W & O/W interfaces. Even PDMSO / PMMA / etc. orient ⟹ L-B like films ∴ clean H_2O ⟹ orientation

also molecular models —
Peloso & Holly
Yasuda
Ratner et al
Cooper et al
Baszkin et al.
more recently: McCarthy / Whitesides
Lavielle —
Ruckenstein

<u>How probe / measure?</u>

XPS — Ratner et al — new facility — cold / hot in situ.
Isotope methods — Ion binding — Baszkin
* Cont ∠ → γ_c / Pennings / Bosman — surf relax t activ E

H_2O ∠s — θ_{Adv}, θ_{Rec}, $\Delta\theta$
Holly / Peloso —
⟹ Underwater contact angles, θ_{rec}.
both — <u>Wilhelmy plate</u>

With Plate — basic principles

hyst loop

Cont. hyst. causes

1. roughness
2. hetero
3. deform
4. overturning
5. entropy / ~~diff~~ mobility

Time effects / relax ?

Modern Modeling

Ruckenstein

Lavalle —

other —

Effects / Expectations

Wetting:

Implic for Protein Ads:

Initial contact.

Later & - dep alteration

Surf. denaturation ?

Implic for Biocompatib

Correlations ?

alkyl surfs
PEO surfs
Prot-Res Surfs

Ongoing work

Concl: H_2O induced restructuring

1. excess
2. t - dependence
3. reversible
4. not whole story.
5. Basic Science ? —

COMPUTER SIMULATION OF LYSOZYME ADSORPTION

J. D. Andrade, J. Herron, V. Hlady*, J. Hansen, and D. Horsley
Department of Bioengineering, University of Utah
Salt Lake City, Utah, 84112, USA

*Institute R. Boskovic, Zagreb, Yugoslavia, 41001

Protein adsorption at solid/liquid interfaces is not well understood, largely due to the great complexity of the process (1). The subject is important to affinity, adsorption, and gel permeation chromatographies; biomaterials blood compatibility (due to surface-induced activation of coagulation and complement); deposits on contact lenses; complement activation and inflammation of intraocular lenses; membrane separation process; food processing; and in protein separation and purification.

Lysozymes are ideal proteins with which to develop models and mechanisms of protein adsorption. Lysozymes are small, well-characterized, enzymatically active, well-understood proteins (2).

We are studying the adsorption of hen and human lysozyme (two very different proteins) on a set of surfaces relevant to the understanding of protein deposition and fouling. Computer molecular graphics have been applied to simulate the adsorption process (3). Interface fluorescence spectroscopy, using extrinsic micro-environment sensitive fluorescent probes, are being used to obtain an understanding of surface-induced conformational changes of adsorbed proteins.

The results are important to the control and perhaps elimination of protein deposits on surfaces and to a better understanding--and prediction--of protein adsorption in general.

Our preliminary results suggest that hen lysozyme may adsorb at hydrophobic surfaces via its surface hydrophobic patch, which is opposite the enzyme active site (3). Such an adsorbed orientation suggests that the enzymatic activity may be retained on the adsorbed state. This hypotheses is now being tested, using a fluorescent substrate for lysozyme and the total internal reflection fluorescence spectroscopy (TIRF) technique (4). The hydrophobic surface patch does not involve tryptophan residues. Thus intrinsic total internal reflection fluorescence spectra of lysozyme adsorption on hydrophobic surfaces may not show significant changes in λ_{max} due to the adsorption process.

Finally as the properties of hen and human lysozymes are different (3), it is likely that the adsorption characteristics of the two proteins may be different. Computer simulation of both hen and human lysozyme indeed shows very different surface structures (5), which are expected to lead to different adsorption properties for the two proteins.

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PHYSIQUE
ET
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29e Cours de Perfectionnement
de l'Association Vaudoise
des Chercheurs en Physique

Saas-Fee, du 22 au 28 mars 1987

Edité par Karin Busch, Christian Depeursinge, Yves de Ribaupierre, Christian Simm

Protein Adsorption and Materials Biocompatibility: A Tutorial Review and Suggested Hypotheses

J. D. Andrade and V. Hlady
College of Engineering, University of Utah, Salt Lake City, Utah 84112/U.S.A.

A comprehensive review of protein adsorption at solid-liquid interfaces is presented, including a brief review of protein structure and the principles of protein adsorption. Adsorption-based biocompatibility hypotheses and correlations are discussed, including surface charge, interface energetics, passivation, protein-resistant surfaces, and the role of adsorbed immunoglobulins and complement. New methods for the study of protein adsorption are discussed, including total internal reflection techniques (absorbance, fluorescence, and Raman) and ellipsometry. Qualitative "rules of thumb" of protein adsorption are also presented.

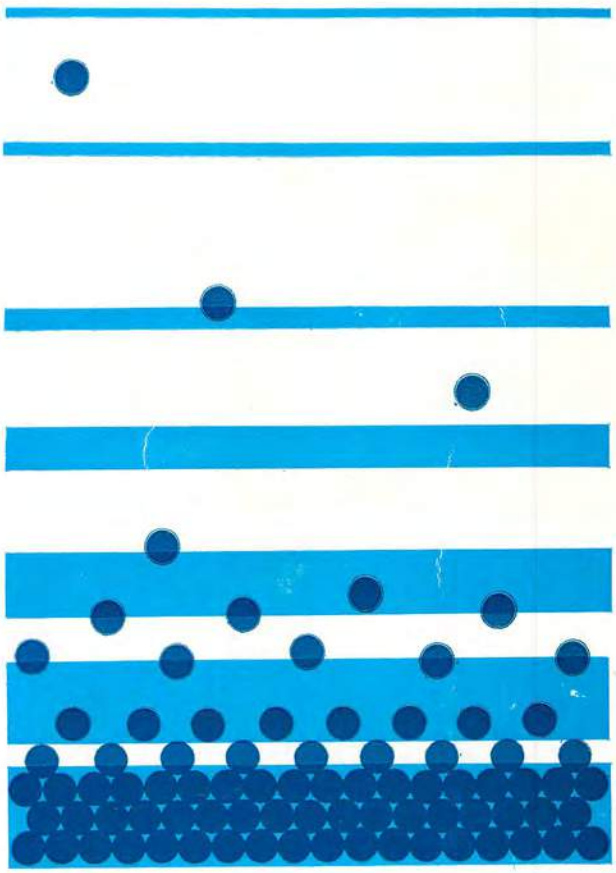
J. Andrade
Utah

VII INTERNATIONAL CONFERENCE

CHEMISTRY OF SOLID/LIQUID INTERFACES

RED ISLAND, ROVINJ

25 JUNE — 3 JULY, 1986.



»RUĐER BOŠKOVIĆ« INSTITUTE
ZAGREB, YUGOSLAVIA

Abstract: International Polymer Biomaterials Symp, Kunming, China May 3-7, 1988

Ab-ANDR-4 China

Competitive Adsorption of Plasma Proteins: A Multi-Channel Approach

J. D. Andrade & V. Hlady*

Departments of Bioengineering and Materials Science
and Center for Biopolymers at Interfaces
University of Utah
Salt Lake City, Utah 84112
USA

*Ruder Buskovic Institute
Zagreb, Yugoslavia

Blood plasma consists of at least 60 and perhaps several hundred different proteins, of which only about 40 have been studied and characterized in some detail (1). Modern quantitative two-dimensional gel electrophoresis (isoelectric focusing and SDS-polyacrylamide gel) of plasma results in at least 600 spots, representing proteins and protein components (2). Proteins are complex macromolecules which are highly surface active. They readily adsorb and concentrate at interfaces by a variety of mechanisms (3-5). There has been much interest and activity in the study of plasma protein adsorption on biomedical polymers in the hope of establishing a correlation between adsorption and the long term blood compatibility of cardiovascular devices (4, 5). Recently, due to an increasinging awareness of the work of Vroman, et al. (6), there has been considerable interest in the competitive adsorption of plasma proteins (4). Brash & Horbett (4) have recently coined the term, the "Vroman Effect", to refer to the competitive adsorption behavior of proteins. There has been some limited success in modeling the Vroman Effect (7, 8). The actual sequence and heirarchy of plasma protein interactions with a surface appear to be dependent on:

1. The particular chemical nature of the polymer surface;
2. The dynamics of the polymer surface (9);
3. The unique structure and surface properties of each of the proteins involved (5);
4. The stability and denaturation properties of each of the proteins involved (10);
5. The liquid medium (pH, ionic strength, temperature, ions, etc.

Our group is addressing these topics.

The nature of the solid surface is characterized by contact angle measurements, x-ray photoelectron spectroscopy (XPS), and inverse gas chromatography (IGC) (see ref. 11). IGC is helpful in obtaining a measure of the partial acid and/or base character of the surface.

Surface dynamics is harder to quantitatively characterize (9). The surface reorientation and restructuring which occurs in going from the air to the aqueous solution environment can be probed via freeze-etch XPS (12), contact angle hysteresis (9, 11), inverse liquid chromatography, and ATR-FT-IR (13). The question that is very difficult to address is how does the polymer surface respond to the adsorbing protein? We have no good way to examine this question, although total internal reflection IR and fluorescence methods offer some hope.

The structure of many proteins is well known and understood (14), especially those proteins whose complete three dimensional structures are known via x-ray crystallography. Using modern computers and molecular graphics programs (15), one can "image" the protein and consider how it may adsorb on a particular surface (3-5, 16). Most plasma proteins are large, globular proteins whose 3-D structures are not known. Our approach to this problem is to use the domain concept of protein structure (14) and to consider the adsorption of plasma proteins in terms of the surface and interfacial properties of their constituent structural domains (7). This approach requires a major commitment to the study and understanding of the structure of each of the plasma proteins of interest.

The stability and denaturation properties of proteins can be assessed by a variety of methods (10). We are examining a set of small, globular proteins of known 3-D structure with the goal of correlating their adsorption properties with structure and denaturation characteristics (17). A multi domain protein often exhibits unique denaturation behavior for each of its component domains. Unfortunately it is not possible even for small, "simple" proteins, to model or simulate denaturation (unfolding) using computer graphics, although progress is being made in the understanding, prediction, and simulation of folding and unfolding of proteins (18).

Even if one knows the structure and dynamics of surfaces and of the proteins, how can one study the competitive adsorption of plasma proteins? This is normally done by radio labelling one protein and then studying its adsorption from plasma (19). This approach is expensive, time consuming, and only practical for examining a small number of interacting proteins. Another approach is to use specific antibodies to probe the concentration and nature of the adsorbed proteins (6, 20). There are many assumptions and problems involved with this method, and it is also impractical if one wishes to look at many different proteins at the same time.

We are beginning to evaluate 2-D gel electrophoresis as a method to measure the concentration of all proteins in plasma as a function of exposure time to polymer surfaces of high surface area. Protein adsorption results in a depletion or decrease of the protein concentration in the solution . The protein solution is sampled as a function of time, and each sample is analyzed by 2-D gel electrophoresis. The different gels are examined using computer methods to determine the solution concentration as a function of time for each of the proteins detected. We have high hopes and expectations for this method.

One aspect of plasma protein adsorption that is often ignored is that the surface-induced enzyme activation which is involved in the activation of coagulation and complement may also result in proteolysis of other proteins. Thus, one expects to see "new" bands appearing and increasing with increasing surface contact. The 2-D gel electrophoresis method permits such processes to be detected and examined.

The study and understanding of plasma protein adsorption is complex and fascinating. Each protein is a unique molecular machine, designed and manufactured for a particular function (21). We must know and understand each of those many different machines if we ever expect to understand. . . and thus to modify and control. . .plasma protein adsorption.

Our work is supported in part by grants from the U.S. National Science Foundation, Army Research Office, National Heart, Lung, and Blood Institute, and by the Center for Biopolymers at Interfaces at the University of Utah.

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ABSTRACT BOOK

XVTH CONGRESS OF
THE EUROPEAN SOCIETY FOR ARTIFICIAL ORGANS

PRAGUE, CZECHOSLOVAKIA, JUNE 29- JULY 1, 1988

ESAO

Thursday, June 30.
Hall B

8.00–8.30 **Invited Lecture:**
S. Stefoni (Bologna): New trends in biocompatiblity evaluation.
Chairmen: P. Ivanovich (Chicago-Rostock)
O. Schück (Prague)

8.30–10.00 **Symposium:**
Biocompatibility: The system approach.
Chairman: H. Klinkmann (Rostock)
Members: J. Bommer (Heidelberg)
B. Schmidt (Munich)
U. Baurmeister (Wuppertal)
R. M. Schaefer (Würzburg)
S. Shaldon (Nîmes)

10.00–10.30 Break

10.30–12.00 **Slide Session B 1:**
Biocompatibility.
Chairmen: U. Baurmeister (Wuppertal)
J. Elis (Prague)

Biocompatibility testing of new vascular prosthetic materials. (A 324)
Walpoth B., Schaffner T., Hoeflin F., Romanello S., Felix R., Althaus U., Markert M., Wauters J., Marquart K., Geroulanos S., Cardiovascular Surgery, Nuclear Med. and Pathology, Berne Univ., Nephrology and Clinical Chemistry, Lausanne Univ., Surgery, Zürich University, Switzerland.

Is monitoring of terminal complement complexes a superior index for bioincompatibility of dialysis membranes? (B 5)
Deppisch R., Schmitt V., Bommer J., Ritz E., Rauterber E. W., Inst. of Immunology and Dept. of Internal Med., Univ. of Heidelberg; Gambro Dialysatoren, Hoechingen, FRG.

Blood response to Cuprophan and Haemophan Membranes. (B 17)
Robertson L. M., Courtney J. M., Travers M., Lowe G. D. O., Bioengineering Unit, Univ. of Strathclyde, Glasgow, Dept. of Med., Royal Infirmary, Glasgow, UK.

Biocompatibility

B1

TITLE QUANTITATIVE 2D GEL ELECTROPHORESIS OF BLOOD PROTEINS

AUTHORS J. D. Andrade, K. Stenelov, H. Chuang, C-H Ho, J. Edwards* and F. Mohammed

ADDRESS College of Engineering, University of Utah, Salt Lake City, UT 84112, U.S.A.
*National Bureau of Standards, Gaithersberg, MD, U.S.A.

There may be over 600 proteins in plasma. They adsorb competitively to medical devices and artificial organs. Although there has been substantial progress in the qualitative understanding of protein adsorption, a quantitative, predicative understanding is still lacking. In some cases trace proteins, such as high molecular weight kininogen, dominate the adsorption process. We are evaluating 2D gel electrophoresis (isoelectric focusing and SDS-Polyacrylamide gel electrophoresis), using quantitative staining, densitometry, and computer-based pattern recognition and comparison techniques, to assess the competitive interaction of all plasma proteins with selected devices and surfaces. Initial results of plasma interactions with high area surfaces will be discussed.

? Fenjen — anticoag effects
E.Leonard — quantit — isotopes
H. Wolf — elution — proteins not eluted?
Leonard ? on stains & staining

B2

TITLE Dialysis-induced eosinopenia: another biocompatibility index?

AUTHORS F.Bergesio, Manescalchi F., Salvadori M., Monzani G., Amato M.

ADDRESS Depts of Nephrology USL 10/D and USL 10/C, Florence, Italy

Thekinetics of eosinophils(E) during hemodialysis and its clinical impl
cations is still controversial. Intradialytic changes in E, leukocytes(
and IgE levels were then examined in 8 patients on chronic hemodialysi
treated with 4 different membranes(Cuprophan, Polyacrylonitrile, Polymet
metacrylate and Polysulphone) both during hemodialysis(HD) and sequenti
ultrafiltration-dialysis(UF-HD). Blood samples were drawn at 0,15,75(UF-
HD) and 240 min. During HD, unlike L,E counts fell significantly regardl
of the type of membrane used and remained low throught the treatment.
When dialysate was bypassed however, eosinopenia was not detectable, and
became apparent again only when the flow was restored. No changes were
found in IgE levels. Our results suggest eosinopenia is secondary to E-
adhesion onto the membranes and seems a dialysate-dependent phenomenon
Dialysis IgE levels and E kinetics are not related phenomenon.
Rather to be a marker of membrane biocompatibility, eosinopenia seems
a usefull index in the more general problem of dialysis biocompatibili

B3

TITLE PLATELETS ACTIVATION IN DIALYSIS: EFFECTS OF MEMBRANE COMPOSITION.

AUTHORS Coli L., Grossi G.*, Bonetti M.*, Borgnino L.C., Stefoni S., Bonomini V.

ADDRESS Nephrology and Dialysis Dept., Centralized Laboratory * - St.Orsola University Hospital - Bologna (ITALY)

Platelet activation is one of the consequence of bioincompatibility of hemodialysis (HD) membranes. To compare the effect on platelets activation of different dialysis membranes, 5 RDT patients were submitted to HD with Cuprophane (CU), Poliacrylonitrile (AN69S) and Polysulfone (PS) hollow fiber dialyzers (total pocedures = 15). Plasma levels of ß-thromboglobulin (ß-TG) and platelets faotor 4 (PF4) and platelet mean diameter (PMD) were measured before HD and after 30', 60' and 240' in arterial and venous lines. In CU HD ß-TG progressively increased with a peak at 60' ($p<0.01$). Values, corrected for hemoconcentration, were significantly higher in venous than in arterial lines ($p<0.05$). PF4 values remained stable during the whole HD session. PMD decreased progressively, with a peak at 240', with lower values in venous than in arterial line; In AN69S HD ß-TG increased progressively with a peak at 240' ($p<0.01$) while PF4 values remained stable. PMD decreased at 30' and 60' with lower values in venous than in arterial line. In PS HD ß-TG showed no significative increases during the session, while PF4 decreased significantly at 240' ($p<0.05$) without arterio-venous differences and PMD showed a low decrease at 240' without arterio-venous differences.

B4

TITLE Are changes in intracranial pressure (ICP) during haemofiltration dependent upon membrane biocompatability?

AUTHORS Davenport A, Losowsky MS, Miloszewski K, Swindells S, Cohen A, Davison AM, Will EJ.

ADDRESS Renal, Liver and Intensive Care Units, St James's University Hospital, Leeds LS9 7TF, UK.

We have previously reported increasing ICP during the first hour of machine haemofiltration (MHF) in patients with grade 4 hepatic encephalopathy and acute renal failure. To determine the importance of membrane biocompatability, we measured the ICP via an intradural catheter in 3 such patients, 2 F, 1 M, age range 23-46 year.

Haemofiltration was performed daily (17L exchange, heparin anticoagulation, blood pump speed 200 ml/min (QB), transmembrane pressure (TMP) 200 mmHg) with either a polyamide or polyacrylonitrite membrane. During 10 MHF treatments with a polyamide filter the mean ICP increased in the first hour from 7.6 ± 1.3 mmHg (mean ± SEM) to 10.3 ± 1.9 mmHg ($P<0.05$), whereas there was no corresponding significant change with 6 polyacrylonitrite membrane treatments (5.5 ± 2.9 mmHg to 6.3 ± 3.4 mmHg). Peripheral wbc and platelet counts and blood gases were measured during treatment with both types of filter. There were no differences in the percentage fall in wbc and PaO2, but the platelet count fell further at 30 min during treatment with the polyamide filter (to 81 ± 4% vs 94 ± 3%, $P< 0.05$).

The differences in ICP during the first hour of treatment using similar QB and TMP and the greater fall in platelet count suggest that membrane biocompatability may play a role in causing raised ICP in these patients.

B9

TITLE ADSORPTION OF ANAPHYLATOXINS C3a AND C5a ON DIALYZER'S POLYVINYL-CHLORIDE BLOOD LINE

AUTHORS A.Kandus*, S.Kladnik**, R.Kveder*, R.Ponikvar*, J.Drinovec*

ADDRESS Departments of Nephrology* and Nuclear Medicine**, University Medical Center, Ljubljana, Yugoslavia

In prospective study, adsorption of C3a and C5a on dialyzer's polyvinylchloride blood line in 7 patients during regular hemodialysis was investigated. Blood samples were taken simultaneously at two points on the output blood line of cuprophan dialyzer 340 cm apart. Blood flow was 200 ml/min throughout study. C3a and C5a plasma concentrations were determined by radioimmunoassay. Results are presented in table ($\bar{X} \pm SD$).

	C3a (ng/ml)		C5a (ng/ml)	
min HD	proximal pt.	distal pt.	proximal pt.	distal pt.
15th	10149 ± 3048	$7275 \pm 2104^{*}$	68.6 ± 39.5	64.8 ± 37.4
60th	4129 ± 1089	3642 ± 382	32.0 ± 3.2	$25.2 \pm 4.9^{**}$
240th	2570 ± 1187	2078 ± 403	13.6 ± 5.4	14.0 ± 2.2

*p<0.05, **p<0.01

Results suggest that significant adsorption of C3a on polyvinylchloride blood line occurred in 15th min of hemodialysis and should be taken into account in assessing dialyzer's membrane biocompatibility. Adsorption of C5a was less pronounced.

B10

TITLE INHIBITORY EFFECT OF PHARMACEUTICALS ON PLATELET ADHESIVENESS ONTO BIOMATERIALS

AUTHORS R. Karwath, M. Schürer and H. Wolf

ADDRESS Humboldt University, Charité, Biomaterials Research Unit & Clinic of Nuclear Medicine, 1040 Berlin, G.D.R.

The reduction of platelet adhesion onto blood contacting biomaterials is considered to be one of the strategies to improve their hemocompatibility. It was the aim of this study to investigate the influence of different pharmaceuticals on the adhesiveness of human platelets onto biomedical polymers.

For quantitative measurements of platelet adhesion an in vitro assessment procedure was used developed recently by us that compares the adhesiveness of Cr-51-labelled human platelets after contact of platelet rich plasma with a biomedical material (poly(vinyl chloride)) and a reference material (glass). The platelet adhesiveness was quantified by means of the "relative index of platelet adhesion".

It was found that the pharmaceuticals: dipyridamole, diazepam and phenylbutazone are capable to cause a concentration dependent inhibitory effect on platelet adhesion onto the surfaces investigated. From these results it was concluded that the inhibition of platelet function by pharmaceuticals seems to be one of the possibilities to improve the hemocompatibility of biomaterials during blood-material contact.

B11

TITLE Granulocyte Related Bioincompatibility of Hemodialysis (HD): Inhibition of Oxidative Metabolism, Degranulation Reaction, Enzyme Release and Leukocyte Sequestration in the Lung.

AUTHORS G. Kolb, H. Schoenemann*, W. Fischer, F. Haydari*, v. Höffken, H. Lange*, K. Havemann; Dept. Hematology/Oncology, *Div. of Nephrology, Univ.Marburg, FRG

It was the aim of this study to evaluate if HD related changes in granulocyte function may depend on the material of the membranes.

Methods: We studied the granulocyte oxidative metabolism during the course of HD by cytochrome C reduction and chemiluminescence. Plasma concentrations of granulocyte (PMN-elastase) were determined as the elastase-a_1-proteinase inhibitor complex (a_1Pi).Distribution of granulocytes during HD was assessed by reinfusion of labeled autologous cells and lung scintigraphy using a computer linked gamma camera. Additionally degranulation reaction during HD with cuprophan and polysulfon was determined by evaluation of a staining score for peroxidase and elastase granule constituents.

Results: Related to the well-known transient leukopenia in the initial phase of HD, PMA-stimulated chemiluminescence (CL) and cytochrome C reduction of granulocytes were inhibited during the first 10-30 min of treatment with cuprophan membranes.Additionally, CL shows a second phase of inhibition after 120 min. Elastase plasma levels increased continuously during cuprophan hemodialysis. In contrast degranulation reactions for peroxidase as well as for elastase could be seen during HD with both, polysulfon and cuprophan membranes. A pulmonary sequestration of granulocytes takes place during the initial phase of HD only with polysulfon. Our data suggest that change in granulocyte function and leukocyte sequestration in the lung may depend on the membrane type of the dialyzer.

B12

TITLE POLYETHYLENE OXIDE SURFACES FOR PROTEIN RESISTANCE AND BLOOD COMPATIBILITY

AUTHORS J-H Lee, P. Kopeckova*, J. Zhang, J. Kopecek*, and J. D. Andrade

ADDRESS College of Engineering, University of Utah, Salt Lake City, UT 84112 U.S.A.
*Institute of Macromolecular Chemistry, CSAS, Prague 6, Czechoslovakia

Plasma proteins adsorb at practically all interfaces. Generally the adsorption process results in activation of coagulation or related processes and therefore requires heparin or other anticoagulant therapy to minimize coagulation and thrombosis. Surfaces which non-specifically repel all proteins are desireable to minimize surface contact activation. Such surfaces are prepared by immobilizing neutral, hydrophilic polymers. The excluded volume and steric stabilization characteristics of these surfaces, well known in colloid chemistry, also result in the entropic repulsion of proteins and thus the minimization of protein adsorption. Polyethylene oxide (PEO) is particularly effective as a steric stabilizer and protein repeller. We have studied PEO surfaces prepared by a variety of methods, including the adsorption of commercial PEO-based block copolymer surfactants. We document the decreased adsorption of plasma and model proteins on such surfaces and suggest mechanisms and explanations for this phenomenon. We discuss contact activation on PEO surfaces and the design of optimal PEO surfaces for enhanced blood compatibility.

Ab-ANDR – 5

Keynote Lecture (3)

PLASMA PROTEIN ADSORPTION: FROM COMPLEXITY TO SIMPLICITY?

J.D. Andrade, A-P Wei, J. Herron, and V. Hlady*

Department of Bioengineering, College of Engineering, University of Utah
Salt Lake City, Utah 84112

Proteins are generally concentrated at adsorbed at air/water, liquid/water, and solid/water interfaces by a variety of interaction mechanisms. Although such interactions can be minimized by appropriate design of the interface, as in the case of neutral, hydrophilic polymer gels, they can also lead to very strong, high affinity, often irreversible binding, as in the case of the conventional polymers and other materials often used as packaging materials, medical devices, and for diagnostic products. General principles of protein structure, particularly the distribution of amino side chains on the surfaces of globular model proteins, will be discussed and correlated to the surface tension (air/water) properties of such model proteins. The surface tension behavior will be correlated with the intrinsic solution denaturability of proteins.

We will attempt to correlate the solution properties with the air/water interface, oil/water interface, and solid/water interface characteristics. We also suggest that the behavior of complex, multi-domain proteins can be treated, in a crude first approximation, by a consideration of the behavior of its individual structural globular domains.

Finally, we will discuss the design of surfaces which actively and sterically repel proteins. Such protein resistant surfaces are of interest in chromatography and medical devices.

Reference
J.D. Andrade and V. Hlady, Adv. Polymer Sci. 79 (1986) 1.
J.D. Andrade, J. Herron, V. Hlady, and D. Horsley, Croatica Chemica Acta 60 (1987) in press.

Partially supported through the Center for Biopolymers at Interfaces, University of Utah.

*Institute Ruder Bos'ovic
Zagreb, Yugoslavi

ABSTRACTS

63rd Colloid and Surface Science Symposium

June 18 - 21, 1989
Seattle, Washington

Sponsored by the
American Chemical Society

in cooperation with

The University of Washington

13 Metastable Conformational States of Proteins at Interfaces. Y.Q. Zhang, J.D. Andrade, A-P Wei, Department of Bioengineering, University of Utah, Salt Lake City, UT84112.

A general theory of conformational change of proteins at the protein solution-air interface is proposed. The relationship between surface tension and time is obtained. Two kind of middle metastable states, backbone middle metastable state and secondary structural middle metastable state are suggested. Processes with few-middle-backbone-metastable-conformational states are analysed in detail. A conjecture about the relation between the number of the extreme points of the surface tension-time diagram and the number of the backbone middle metastable states is given. The theory is fitted with the experimental data obtained from Lysozyme, Ribonuclease-A, Myoglobin, Cytochrome-c and Superoxide dismutase solutions-air interfaces. We find that Lysozyme and Superoxide dismutase could have backbone middle metastable conformational states. Ribonuclease-A, Myoglobin and Cytochrome-c could have middle secondary structural metastable conformational states. The decay constants of the conformations of model proteins are not constants due to the time-dependent microenvironmental changes of proteins at the interfaces. A semiempirical formula is proposed to describe the experimental data.

14 MOLECULAR LEVEL STUDY OF PROTEINS ON SURFACES THROUGH FT-IR AND LANGMUIR-BLODGETT MONOLAYER TECHNIQUES. Krishnan K. Chittur, Corazon A. Steginsky. The National Center for Biomedical Infrared Spectroscopy, Battelle's Columbus Division, 505 King Avenue, Columbus, Ohio 43201-2693.

The composition and the physical state of proteins adsorbed onto biomaterial surfaces play an important role in cellular interactions leading to thrombogenesis. In addition to obtaining information about the kinetics of protein adsorption, conformation information is obtained by quantifying changes in bands corresponding to a number of secondary structures like the alpha-helix and beta-sheet. Comparison of polarized ATR spectra of adsorbed fibrinogen with polarized ATR spectra of Langmuir-Blodgett monolayers of fibrinogen transferred to substrates allows a description of the orientation of protein molecules on surfaces. Our experiments with fibrinogen indicate that both the kinetics of adsorption and conformation of proteins is a function of the wall shear rate and the type of adsorbing surface. Analysis of the changes in the dichroic ratios suggest that molecular orientation may also be surface dependent. Development of these techniques thus allows us to probe protein-surface interactions at the molecular level. This work was supported in part by Grants RR-01367 and HL-38936 from the National Institutes of Health.

15 INTERFACIAL ENERGETICS OF PROTEINS. Wendy C. Duncan-Hewitt, Zdenka Policova, Walter Zingg, and A. Wilhelm Neumann, Department of Mechanical Engineering, University of Toronto, 5 King's College Road, Toronto, Ontario, M5S 1A4, Canada.

The purpose of this paper is to initiate consideration of protein conformation at interfaces through the analysis of interfacial energetics. Our immediate object is to compare the surface free energies of proteins at the water/air interface with those of proteins which are adsorbed onto solids. While the latter measurement, derived from contact angle values, are well in hand through our recent development of Axisymmetric Drop Shape Analysis, the deceptively simple issue of measuring the liquid/air interfacial tensions of protein solutions is confused in that different methods produce results which do not agree. We shall elucidate this problem and present a comparison of the energetics of human serum albumin, fibrinogen, and other common plasma proteins in the two interfacial systems.

16 DRUG POLYMER ASSOCIATION IN NANOPARTICULAR SYSTEMS. CHARACTERIZATION OF INTERFACIAL PROPERTIES BY SURFACE PRESSURE AND SURFACE POTENTIAL MEASUREMENTS. M. Deyme, A. Baszkin, P. Couvreur, G. Albrecht, Physico-Chimie des Surfaces et Innovation en Pharmacotechnie, CNRS UA 1218, Université Paris-Sud, Chatenay-Malabry, France.

Surface pressure-area isotherms of poly(alkylcyanoacrylate)/drug monolayers spread at the air-water interface, obtained in dynamic conditions using a Langmuir film balance, reveal that polymer/drug interactions are enhanced when the monomers are polymerized in presence of adjuvants.

These experiments, performes with poly(isobutylcyanoacrylate) and ampicillin, clearly show that the association between the drug and the adjuvant free polymer is weak and can be easely disrupted. This association is strong enough to resist high compression in the case of the adjuvant loaded polymer.

Surface pressure and surface potential studies of poly(isobutylcyanoacrylate) monolayers, performed in equilibrium conditions, confirm an important role played by the polymerization adjuvants (glucose and dextran) in forming polymer-ampicillin association.

Based on these experiments, models of poly(isobutylcyanoacrylate)/ampicillin arrangements in the interfacial region are proposed for the low and high polymer surface densities.

Molecular Basis of Surface activity

17 ADSORPTION OF MODEL PROTEINS AT THE AIR-WATER INTERFACE:ROLE OF STABILITY AND EFFECTIVE HYDROPHOBICITY. Ai-Ping Wei, James N. Herron, Joseph D. Andrade. Department of Bioengineering, The University of Utah, Salt Lake City, Utah 84112

A set of small,single domain proteins, including cytochrome-c, myoglobin, lysozyme, ribonuclease-A and superoxide dismutase, were chosen as model proteins to study the relationship between their structures and adsorption behavior. The surface tensions of solutions (0.1 mg/ml in PBS buffer) of these proteins were measured as a function of time by the Wilhelmy Plate technique. The intrinsic stabilities were fluorimetrically determined by guanidinium hydrochloride(GdnHCl) denaturation in solution. The effective surface hydrophobicities were probed by a fluorescent hydrophobic probe, cis-parinaric acid. The measured surface tension values at the adsorption time of less than one minute correlate very well with the probed effective surface hydrophocities. The surface tensions under denaturing conditions(8M GdnHCl) correlate well with the apolar amino acid residues content, while the equilibrium surface tensions did not show any significant correlation with either of these two parameters. It is proposed that both the intrinsic stability and effective surface hydrophobicity of a protein are significant in determining the extent to which it adapts its conformation to a surface. Experimental results are examined by computer molecular graphics and calculations of accessibility based on the x-ray coordinates.

? b/l Paul Yager on control of surf. pressure & effect of π on surface denat'n rate. —

* reach calc'n of ads E ~ same as ΔG denat'n in sol'n

18 COMPETITIVE AND SEQUENTIAL ADSORPTION OF MODEL PROTEINS.
T. Arai, H. Shirahama and W. Norde, Wageningen Agricultural University, Department of Physical and Colloid Chemistry, P.O. Box 8038, 6700 EK Wageningen, The Netherlands

The proteins used in this study, lysozyme (LSZ), ribonuclease (RNase), myoglobin (MGB) and α-lactalbumin (αLA) have comparable low molecular masses (ca. 15,000 Dalton) and similar dimensions but they differ with respect to isoelectric point and structure stability. Competitive and sequential adsorption experiments have been performed in a systematic way, using sorbent surfaces of varying hydrophobicity and charge density. Information has been derived from depletion measurements, electrophoresis, streaming potential measurements and reflectometry. The conclusions may be summarized as follows.

1. For a given surface adsorption preference between LSZ, RNase and MGB tends to be determined by electrostatic interactions. With αLA an extra factor, related to the low structure stability of this protein, contributes to preferential adsorption.
2. Sequential adsorption of LSZ, RNase and MGB occurs on surfaces precoated with a different protein, only if it is electrostatically favorable. Sequential adsorption of αLA occurs under all conditions of electrostatic interaction.

Hard vs Soft proteins soft : readily denatures

69 INVERSE GAS CHROMATOGRAPHY AS A METHOD FOR EXPLORING SURFACE PROPERTIES OF BIOMATERIALS. K.M. Sibrell, K.D. Caldwell, J.D. Andrade, Department of Bioengineering, Center for Biopolymers at Interfaces, University of Utah, Salt Lake City, Utah, 84112

The interfacial free energy of a biomaterial, when in contact with biological solutions is generally considered to be an important determinant in biocompatibility. It is difficult, however, to directly measure the surface energies of polymers immersed in solutions. Inverse gas chromatography (IGC) provides a method for measuring surface energies of materials in terms of a non-polar, and an acid/base or polar component. Although not directly relevant to the biocompatibility question, these surface characteristics have potential use in comparing the performance of different materials. Application of the IGC technique to materials of biomaterials interest such as polyurethanes, polytetrafluoroethylene (PTFE) and pyrocarbons will be discussed. Short-chain alkanes are used as probe molecules to determine the non-polar surface energy component. The usefulness of alcohols, amines and other previously characterized molecules is examined to assess the acid/base character of the materials. In addition, thermally induced changes such as glass transitions and relative surface domain sizes of multi-phase materials will be explored.

70 **FRONTAL CHROMATOGRAPHIC ANALYSIS ON DYNAMIC BEHAVIOUR OF PROTEINS AT POLYMER SURFACE**

Y.Tashiro, T.Tsuruta, K.Kataoka*, Y.Sakurai*
Dept. of Industrial Chemistry, Science University of Tokyo, Tokyo 162, JAPAN
*Institute of Biomedical Engineering, Tokyo Womens' Medical College, Tokyo 162, JAPAN

Protein adsorption plays an important role in interaction of biological substances with biomedical materials. The purpose of this study is to clarify an effect of hydrophobicity of polymer materials on the status and process of protein adsorption. Frontal chromatography is applied to get insight into the mechanisms of protein adsorption and subsequent conformational change at polymer surfaces. The amount of bovine serum albumin and immunoglobulin G (IgG) adsorbed on polystyrene was found to be less influenced by flow conditions, suggesting a formation of stable protein layer even in an initial stage of adsorption due to considerably strong hydrophobic interaction. On the other hand, IgG adsorption on poly(2-hydroxyethyl methacrylate)(PHEMA) was crucially affected by feeding condition of IgG into PHEMA column: the amount of IgG adsorbed was increased with an increase in concentration and feeding rate of IgG. This increase could be explained by considering a differential contribution of adsorption rate of IgG onto PHEMA surface and rate of subsequent stabilization process of adsorbed IgG molecules, including change in orientation and conformation.

71 A NOVEL NATURAL POLYSACCHARIDE WITH POTENT ANTITHROMBIN ACTIVITY. S. Colliec[a], C. Boisson-Vidal[b], A.M. Fischer[b], J. Tapon-Bretaudiere[b], P. Durand[c] and J. Jozefonvicz[a]
a/ L.R.M.,C.S.P.,U.P.N.,Av J.B. Clément, 93430 Villetaneuse France,
b/ Laboratoire d'hématologie, Hôpital Necker-Enfants-Malades, 154 rue de Vaugirard, 75015 Paris, France.
c/ IFREMER Rue de l'Ile d'Yeu, B.P. 1049, 44037 Nantes, France.

Heparin has been used in anticoagulant therapy for more than forty years. This drug heterogeneous both in its chemical composition and its molecular weight, is the oldest antithrombotic drug still in use and remains the most widely used agent for immediate anticoagulation. However, there is now a tremendous interest in research for sulfated polysaccharides showing anticoagulant properties. Since 1930, numerous natural or synthetic heparin-like substances have been studied such as fractionated heparin, dextran sulfate, heparan sulfate, pentosan sulfate and dermatan sulfate. The purpose of all these studies is to obtain new antithrombotic homogeneous drugs, better characterized than heparin, with lower bleeding complications and a less expensive manufacturing cost. Our study is focused on fucoïdans, sulfated polysaccharides extracted from the cell wall of marine brown algae, which exhibit anticoagulant activities. We choose to further investigate the mechanism of their anticoagulant potency.

72 THE CHEMICAL COMPOSITION, PARTICLE SIZE RANGE, AND BIOLOGICAL ACTIVITY OF SOME LMW HEPARIN PREPARATIONS. George A. Neville and Fred Mori, Health Protection Branch, Health and Welfare Canada, Ottawa, ON, K1A 0L2; Thomas J. Racey and Paul Rochon, Dept. of Physics, Royal Military College of Canada, Kingston, ON, K7K 5L0; Kevin R. Holme and Arthur S. Perlin, Dept. of Chemistry, McGill University, Montreal, PQ, H3A 2A7.

Several low molecular weight (LMW) heparin sodium preparations from different sources, as well as some related regular heparin sodium preparations, were examined for chemical composition by high field (300 MHz) ^{1}H-NMR spectroscopy, for particle size range by quasi-elastic light scattering (QELS) methods, and for anti-coagulation potency and anti-factor Xa activity by the standard US Pharmacopeial assays prescribed for regular heparin. The NMR spectra provided insight into the mode of depolymerization used to generate the LMW heparins as well as to the presence of dermatan sulfate or other chemical contaminants. QELS analysis permitted the heparin preparations to be characterized and compared by virtue of their distinctive particle size distributions.

73 ADSORPTION OF HEPARIN BINDING PLASMA PROTEINS STUDIED BY 2-D GEL ELECTROPHORESIS

C-H. Ho, J. D. Andrade and C. Stenelov, Dept.of Materials Science & Engineering and Center for Biopolymers at Interfaces, University of Utah, Salt Lake City, Utah 84112

Many plasma proteins adsorb to non-physiologic interfaces and can induce blood coagulation, an important factor in the biocompatibility of biomaterials. Heparin is a heterogeneous sulphated glycosaminoglycan with anticoagulant activity. Several plasma proteins interact with heparin, such as antithrombin III, fibronectin, vitronectin, lipoproteins and complement. Heparin can enhance the binding of antithrombin III to thrombin to prevent blood coagulation; antithrombin III is the strongest heparin-binding plasma protein. The concentration of antithrombin III in normal human plasma is 20-40 µg/ml. By using high resolution, two-dimensional (2-D) gel electrophoresis (isoelectric focusing and SDS-PAGE), we are studying the competitive interaction of heparin-binding plasma proteins with selected anionic surfaces. From the 2-D gel, we can clearly identify the plasma proteins by comparison against purified standards. Also, by using quantitative staining, densitometry and computer aided analusis, we can quantify the plasma protein pattern in the gel.

74 ADSORPTION OF FIBRINOGEN ON ALKYL-AGAROSES, H.P. Jennissen and A. Demiroglou, Institut für Physiologie, Physiologische Chemie und Ernährungsphysiologie, Universität München, Veterinärstr. 13, D-8000 München 22, West Germany

Our protein adsorption studies have been performed on alkyl derivatives of agarose (Sepharose 4B) gels, which on scanning electron micrographs [1] have been shown to consist of pores (mean diameter 150-200 nm) and non porous dense areas (over 100 x 100 nm in size) probably comprising the surface area available for protein adsorption. From the cooperative and hysteretic adsorption behavior of proteins on alkyl [illegible] it has been concluded (for review see ref. [2]) that the adsorption process is not ther[illegible] hypothesis of protein adsorption).

Paper withdrawn

The adsorption of fibrino[illegible] alkyl Sepharoses (carbamate and thioether linked). Adsorption strongly depends on the surface concentration and the length of the immobilized alkyl residues and is of much higher affinity on the thioether than the carbamate linked agarose derivatives. This behavior is similar to that obtained with the globular proteins calmodulin and phosphorylase b.

[1] Jennissen, H.P., Demiroglou, A. and Kerfin, W. (1987) J. Cell. Biochem. 35, 3
[2] Jennissen, H.P. (1988) Makromol. Chem., Macromol. Symp. 17, 111-134

Use 3D sides!

139 SCANNING TUNNELING MICROSCOPIC STUDIES OF CARBON MATERIALS, INCLUDING AMINO ACIDS AND PROTEINS ON HIGHLY ORIENTED PYROLYTIC GRAPHITE. L. Feng, C-Z Hu and J. D. Andrade, Dept. of Materials Science and Engineering and Center for Biopolymers at Interfaces, University of Utah, Salt Lake City, UT 84112.

We present our studies of scanning tunneling microscopy (STM) on (1) pyrolytic carbons and highly oriented pyrolytic graphite (HOPG), (2) four amino acids, gly, leu, met and trp, adsorbed on HOPG, and (3) three proteins, hen lysozyme, human albumin and human fibrinogen, deposited on HOPG. STM provides the opportunity to probe the surfaces and adsorbates with high resolution, surface sensitivity, 3-dimensional character, and in a nearly native environment. STM images of pyrolytic carbon show its surface topologies and some graphitic domains. Amino acids have different adsorbing patterns, partially dependent on their molecular sizes. Finally, STM observations of the adsorbed proteins give some instructive results, including the domain structure of albumin and motion of fibrinogen molecules on HOPG.

140 **INTERFACIAL TENSIONS AND CONTACT ANGLES BY AXISYMMETRIC DROP SHAPE ANALYSIS.**
A.Wilhelm Neumann, Philip Cheng, Frank DeFilippis, Dongqing Li, Zdenka Policova, and Wendy C. Duncan-Hewitt. Department of Mechanical Engineering, University of Toronto, Toronto, Ontario, M5S 1A4, Canada.

will send review preprint

Liquid/fluid interfacial tensions and contact angles are readily determined with great precision using Axisymmetric Drop Shape Analysis (ADSA), an image analysis based procedure whereby surface and interfacial tensions are calculated from the shape of pendant or sessile drops. A video image of a drop is transferred immediately to a digitizer where it is digitized to a 480 x 512 pixel array with 256 gray levels thereby avoiding the error associated with photographs or other intermediate imaging procedures. Subsequently the profile coordinates are determined using an automatic edge detection scheme. ADSA is then employed to calculate the interfacial tension and/or contact angle by fitting a LaPlacian curve to an experimental drop profile by adjusting the putative value of the interfacial tension. Apart from the local gravity and the densities of the liquid and fluid phases, only the experimental drop profile coordinates are required as input information. The range of applicability of this technique will be illustrated by the following: 1) evaluation of the pressure dependence of liquid/fluid interfacial tensions; 2) drop-size dependence of contact angles and line tensions; 3) adsorption kinetics of surfactants at the air/water interface; 4) contact angles of water on layers of biological cells and proteins.

141 FULLY AUTOMATIC SURFACE TENSION AND CONTACT ANGLE MEASUREMENT, Udo Uhlerich, Tekmar Company, PO Box 371856, Cincinnati, Ohio 45222-1856

No good.

Surface tension and interfacial tension of solids and liquids are of fundemental importance for the understanding of emulsification, washing, foaming, wetting and similar surface related processes. Due to increased quality standards and the new problems posed, the requirements of accuracy and operating speed of the measuring instruments have risen remarkedly. The measurement of contact angles and the calculation of critical surface tension of solids is especially challenging considering the polar and dispersive effects on the data creating some error. Our contact angle measuring system allows fast computer controlled contact angle measurements, the automatic calculation of critical surface tension and the calculation of polar and ~~dispersive effects~~.

The processor controlled tensiometer enables fully automatic measurements of surface and interfacial tension of liquids. In combination with a dosimat the tensiometer is able to measure critical micelle concentrations (CMC) automatically with day and night operation at an accuracy of 0.01mN/m!

188 STABILITY OF A BINARY COLLOIDAL SUSPENSION AND ITS EFFECT ON COLLOIDAL PROCESSING. Wan Y. Shih, Jun Liu, Wei-Heng Shih, Ryoichi Kikuchi, and Ilhan A. Aksay, Dept. of Materials Science & Engineering, Univ. of Washington, Seattle, WA 98195.

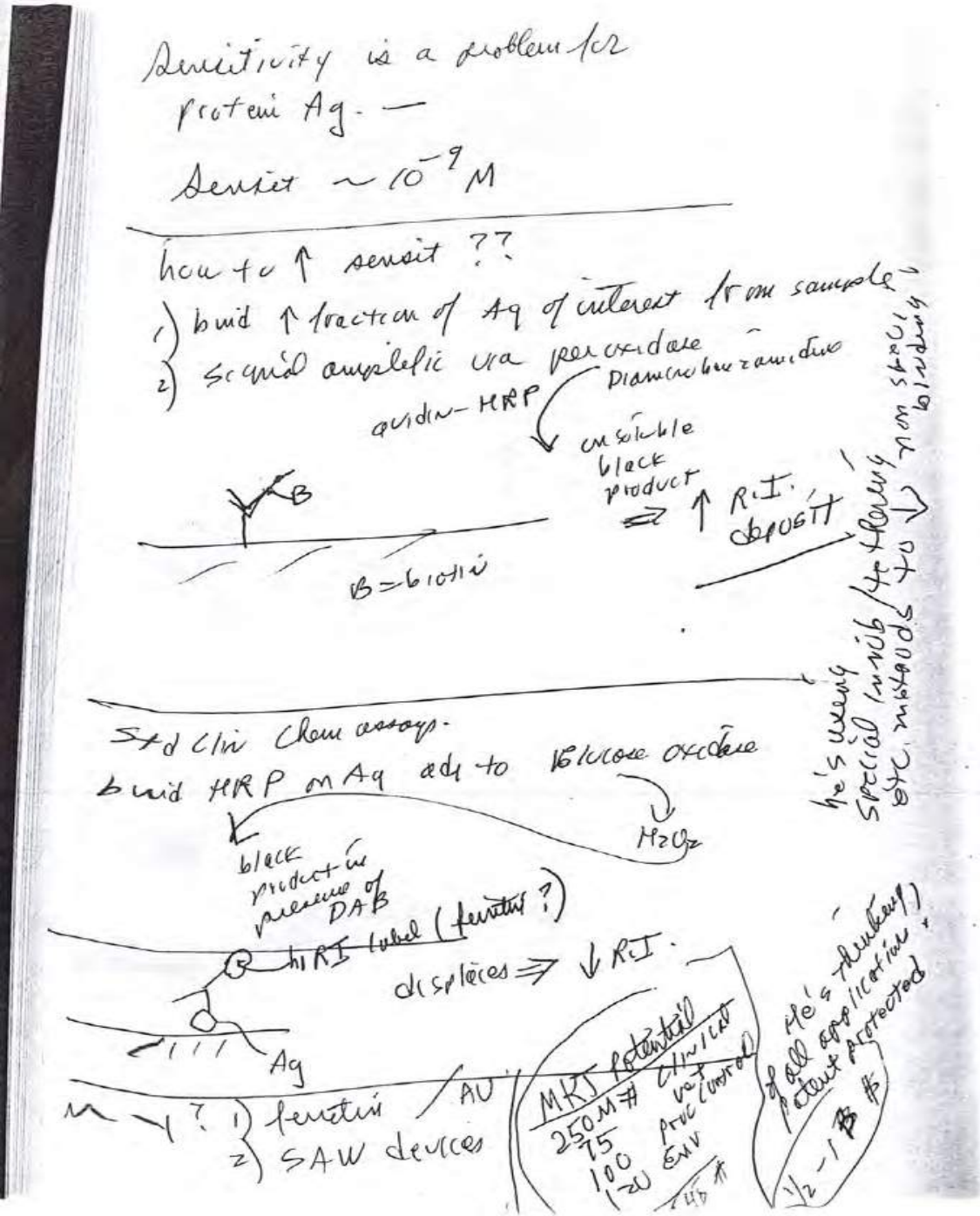
The stability of a binary colloidal suspension was examined by means of analytic calculations as well as numerical simulations. (1) When interaction between all particles is dominated by Coulomb repulsion, the suspension may change from a "fluid" phase to a "solid" phase via freezing when parameters such as total particle volume fraction, the volume fraction of one of the species, the salt concentration or the pH are varied. By directly comparing the free energies of the solid phases and the fluid phase through the construction of solid-fluid phase diagrams, we found that there is always a maximum freezing density when the volume fraction of one of the species is varied, which would imply a maximum green density in colloidal processing. (2) In the weakly attractive regime, the interaction is repulsive for one of the species and slightly attractive for the other. We studied the flocculation behavior of the slightly attractive species through extensive Monte Carlo simulations and analytical calculation, and found that there is a maximum flocculation rate when the density of the repulsive species is varied while the density of the slightly attractive species is held constant, which is in good agreement with experiment and implies that there is a minimum green density in this regime in colloidal processing.

189 THE DISTRIBUTION OF BINDING SITES ALONG THE WETTABILITY GRADIENT ON THE MODIFIED SILICA SURFACE. V. Hlady, Y.S. Lin and J. D. Andrade, Center for Biopolymers at Interfaces, Department of Bioengineering, University of Utah, Salt Lake City, Utah, 84112

The surfaces with some gradient-like varying characteristics are finding an increased use in protein adsorption studies. One of such surfaces is the silica surface with the wettability gradient which can be prepared by two-phase solution silanization using dichlorodimethylsilane (DDS). Although the contact angle of such surface changes smoothly from approx. 0 to 88 degree, the adsorption/desorption experiments done with some proteins show unexpected results at the middle portion of the gradient. Several methods of fluorescence spectroscopy were used to analyse the degree of heterogeneity of the binding sites distribution along the wettability gradient. The spectroscopic mapping of the gradient was achieved employing the total internal reflection fluorescence geometry combined with the CCD detection of the fluorescence emission of adsorbed fluorescent polarity probes.

190 ADSORPTION OF THREE PLASMA PROTEINS ON THE SILICA SURFACE WITH WETTABILITY GRADIENT. C.G. Gölander, V. Hlady, Y.S. Lin and J. D. Andrade, Center for Biopolymers at Interfaces, Department of Bioengineering, University of Utah, Salt Lake City, Utah, 84112

The adsorption of three plasma proteins on the modified silica surface was studied by total internal reflection fluorescence (TIRF) method. The surface was prepared by two-phase solution silanization using dichlorodimethylsilane (DDS) and showed a smooth gradient of wettability along one dimension. The adsorption of FITC-labeled proteins: albumin, immunoglobulin and fibrinogen was carried out from a single protein solution and from a mixture. The single protein adsorption experiment showed that the protein affinity for the surface remains unchanged along the wettability gradient; immunoglobulin > fibrinogen > albumin. The adsorbed amount was larger at the non-wetting side of the gradient. The adsorption from protein mixture showed that after 120 minutes of contact time the silica surface is largely depleted of adsorbed immunoglobulin. The elutability of adsorbed protein was tested using a non-ionic surfactant solution.



BI.01 PROTEINS AT INTERFACES: PRINCIPLES AND APPLICATIONS.

Andrade J.D., Hlady V., Herron J., Lin J-N., Wei A.P., and Feng L.

Department of Bioengineering.University of Utah.Salt Lake City.Utah 84112 USA

Proteins are nature's molecular machines. There is considerable interest and activity in applying and adapting proteins for the development and application of biomolecular devices and machines (1). Such applications require the handling and processing of proteins, including their concentration, ordering, and assembly at interfaces. Protein interfacial properties are also important in the biocompatibility of medical devices and in protein processing for biotechnology purposes. The current principles and understanding of proteins at interfaces are presented and reviewed, including current theories and hypotheses.

INTRODUCTION TO PROTEINS (2,3)

Proteins range in size from several thousand (10^3) to tens of millions (10^7) Daltons. The structure of globular proteins is generally only marginally stable, partially unfolding to a "denatured" state with a free energy input or change of only 5-15 k cal/mole. Large proteins generally consist of several structural and functional domains. Complex proteins are now believed to consist of domain "building blocks".

Practically all proteins are polymeric surfactants in aqueous solution. Their constituent amino acids have hydrophobic and hydrophilic (neutral, positive, or negative) character, and hydrophobic interactions are very important in their globular stability and in their interfacial activity. It is now generally accepted that the placement of proteins at interfaces, usually via adsorption from solution, results in a conformation and orientation different from that under "normal" physiologic conditions. Such interface microenvironment -- induced altered states can result in "abnormal" or unexpected biochemical and biophysical properties. Several well known examples are the interface-induced activation of blood coagulation, activation of the complement defense system, activation of inflammatory processes, and enzyme inactivation.

PROTEIN ADSORPTION

A number of recent conference proceedings and an edited monograph are now available (4-6), as well as several comprehensive reviews (7-9). The following general principles and hypotheses are now accepted and being tested (Figure).

1. Each protein has its own distinctive and individual "surface"

chemistry produced by the outer shell of amino acids and carbohydrate which interface with the liquid medium (7,11). (Figure a)

2. Diffusion or convective transport results in a collision rate between proteins in solution and the interfaces present (7,10). (Figure b)

3. Although protein molecules collide with the interface in many different possible orientations, one specific orientation will probably result in the most stable adsorption, with hydrophobic surface patches oriented towards hydrophobic interfaces, anionic patches oriented towards cationic surfaces, etc. (Figure c) Domain and mosaic surfaces can be expected to have rich and complex interactions with the domains and mosaics on the surface of the protein.

4. If the collision rate is very high and the interface is populated with protein very quickly, the proteins may not show extensive time-dependent denaturation processes (figure d), although there may be some adjustments in packing, ordering, and lateral interactions (4-7).

5. If the surface is not highly populated, the adsorbed protein may denature and/or spread at the interface, altering its conformation and orientation to optimally adjust to its new microenvironment. (Figure d) Such events may result in the expulsion of less optimally oriented or bound proteins from the interface, as the more optimally oriented or bound protein spreads at the interface. (Figure e) The tendency for the protein to denature at the interface is related to its intrinsic stability, including the number of disulfide bonds (12).

6. The presence of two or more different proteins in the solution will result in competitive adsorption processes; with that protein which can most optimally bind and accommodate at the interface tending to displace its less optimally bound neighbors (figure e,f). Thus, a complex hierarchy of adsorbed protein types and amounts can develop with time, related to solution concentration, size, collision rates, interface affinity, and denaturation tendencies. This behavior is now called the "Vroman Effect" (12,13).

7. It is possible to control and regulate protein adsorption, in part, by modifying the surface or interface or by modifying the protein, such as with steric exclusion modifiers (14,15). (figure g)

8. Materials and interfaces with a micro-heterogeniety of the same size as the structural domains or building blocks in proteins probably have a particularly rich and complex set of adsorption properties. (figure h)

CONCLUSIONS AND PROSPECTS

These general concepts and hypotheses provide some appreciation

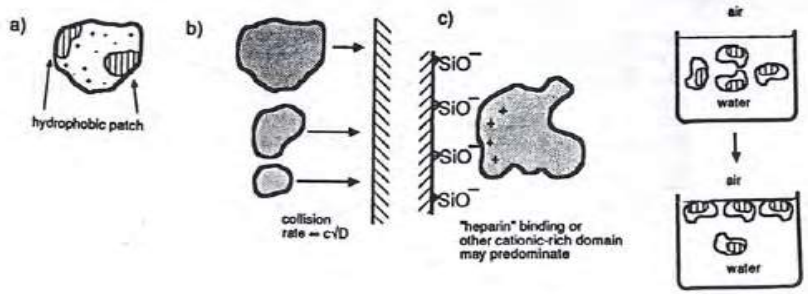
and qualitative understanding of protein interfacial processes. There is considerable progress on the modeling and simulation of selected interfacial properties by several groups (7,8,16-17) Due to the complexity of the general adsorption process, however, a quantitative, truly predictive model for complex multi-component systems will not be available in the near future.

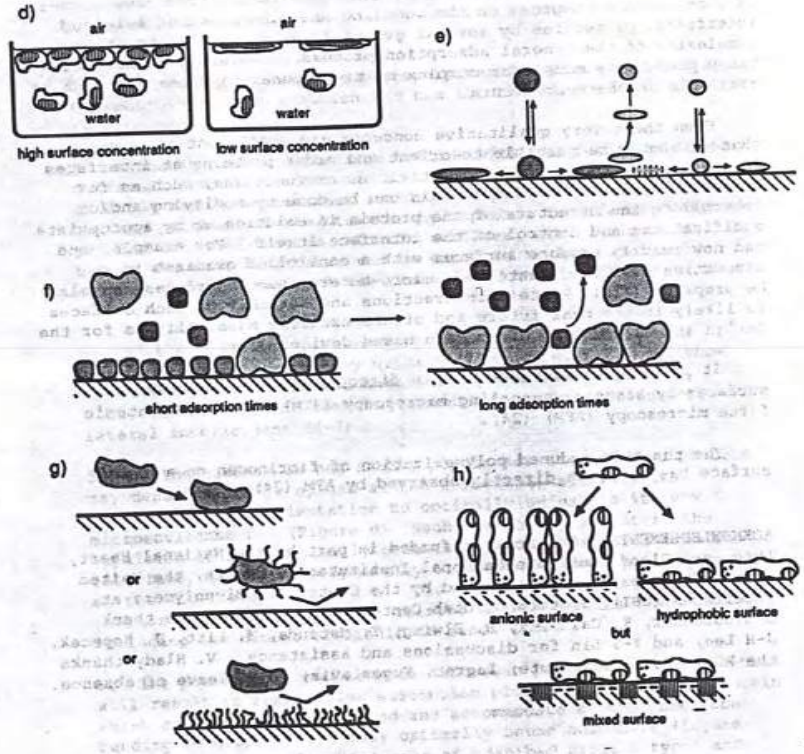
Even these very qualitative concepts are sufficient to suggest that it should be possible to orient and order proteins at interfaces in order to optimize specific activities or functions, such as for biosensor applications (18). This can be done by modifying and/or controlling the structure of the protein in solution or by appropriate modifications and control of the interface itself. For example, one can now readily produce surfaces with a controlled gradient in properties (19,20). Patterned, micro-heterogeneous surfaces can also be prepared (21). Protein interactions and assembly on such surfaces is likely in the near future and offers exciting possibilities for the design and fabrication of protein based devices (27).

It is now becoming possible to directly observe proteins on surfaces by scanning tunneling microscopy (STM) (23) and by atomic force microscopy (AFM) (24).

The thrombin-induced polymerization of fibrinogen on a mica surface has now been directly observed by AFM (24).

ACKNOWLEDGEMENTS: Our work is funded in part by the National Heart, Lung, and Blood Institute-National Institutes of Health, the United States Army Research Office, and by the Center for Biopolymers at Interfaces (CBI), a State of Utah Center of Excellence. We thank C.G.Golander, K. Caldwell, H. Elwing, T. Matsuda, W. Pitt, J. Kopecek, J-H Lee, and Y-S Lin for discussions and assistance. V. Hlady thanks the R. Boskovic Institute, Zagreb, Yugoslavia, for a leave of absence.





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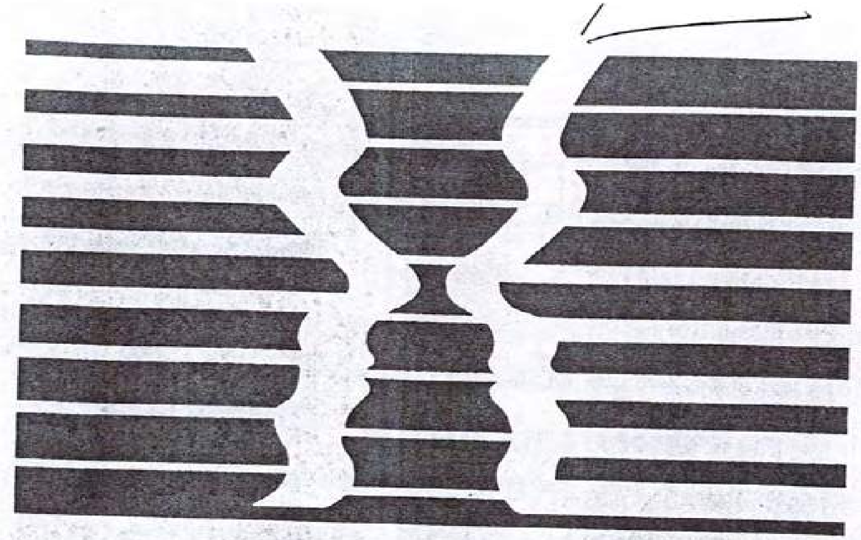

Bio Science

Abstracts

Volume 2 : 1989

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Int. Soc. Tech Assess. Health Care
May 20-23, 1990 Houston

Title: Bioengineering Approaches to Decreasing the Cost of Health Care Paper ☒ Poster ☐

Author(s) & Degree(s): J.D. Andrade*, Ph.D., R.P. Huefner, D.B.A. J. Williamson, M.D., B. James, M.D., R. Helmer, M.D.

Mailing Address & Telephone #: University of Utah, Department of Bioengineering, 2480 MEB, Salt Lake City, UT 84112, (801) 581-4379

The rapidly increasing cost of health care in the United States is now a subject of considerable interest and concern for all segments of society. Historically the academic bioengineering community has not been particularly concerned with the cost implications of the technologies and instruments which it develops. The medical community, which applies the results of bioengineering research and development, has also been generally unaware and unconcerned with cost considerations until relatively recently. The situation of course has changed dramatically in recent years. We feel strongly that at least a portion of academic bioengineering education, research, and development be directed to the health care cost issue.

The graduates of academic bioengineering programs nationally go on to work in the health care products industry, in government regulatory bodies, and in academia. Students in bioengineering programs should be induced to consider the cost - benefit implications of their graduate research work and should have some general familiarity with the concepts and techniques of technology assessment and cost benefit analysis.

We are in the process of establishing a course on Bioengineering and the Cost of Health Care, to be taken by a wide range of graduate students at the University of Utah, including students in the Bioengineering program. It is our expectation that this course will become a permanent part of the curriculum and that the principles and concepts of the course can be expected to be integrated into other courses and, hopefully, into every graduate student dissertation. In addition, we are setting up a clinical bioengineering internship program to enable interested students to work closely with major primary health care providers in the Salt Lake City area to learn first hand their need and problems.

We want to take a global look at primary medical care activities and to evolve new and novel approaches which could have a significant impact on decreasing health care costs. This program is an experiment and is only now being initiated. It merits careful attention and consideration as it is likely that technology and engineering can be applied in new and novel ways to help solve, rather than to exacerbate, the problem.

* To whom correspondence should be directed.

Bioeng in Society/Educ

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BMES Abstract

Using Bioengineering for Science Education

J.D. Andrade
Department of Bioengineering, 2480 MEB
Salt Lake City, Utah 84112

There is growing interest in enhancing science and technical education at all levels in our society and particularly for the general public.

Among the greatest motivators of our population are the topics of sports, sex, and health. All three of these natural motivators are directly related to bioengineering. The general public in science museums and science centers and students in schools are highly motivated by experiments which involve their own body. It is clear that simple, safe measurements of a variety of physiological functions can be used as motivators and as sources by which to develop science and technical education concepts.

A group of bioengineering graduate students enrolled in a special projects course to develop and apply physiologic measurements, made very simply, inexpensively and safely, to demonstrate and develop a variety of science and technical principles and applications.

Simple measurements and experiments were used as a vehicle to develop a wide range of science concepts and skills of increasing levels of depth and sophistication.

AB-
ANDR - 14

A2 / P-34 :

MANIPULATION OF SURFACE-ADSORBED PROTEINS BY ATOMIC FORCE MICROSCOPY.

J.D. ANDRADE[1], A.S. LEA[1], A. PUNGOR[1], V. HLADY[1], J.N. HERRON[1], E.W. VOSS Jr [2].

1 University of Utah, Department of Bioengineering, SALT LAKE CITY, UT 84112, USA.

2 University of Illinois at Urbana-Champaign, Department of Microbiology, URBANA, IL 61901, USA.

The atomic force microscope was used to visualize protein adsorption in real time. Antifluoresceyl murine monoclonal IgM (18-2-3) was adsorbed from buffer solution onto the muscovite mica surface. When the cantilever of the microscope was scanning continuously one scan area, even with the smallest attractive force of ≈ 4nN we could achieve, the adsorbed IgM was observed to be rapidly manipulated into strands oriented perpendicularly to the fast scanning direction of the microscope. This observation suggested that only a weak adhesion existed between the adsorbed protein and the mica surface. By increasing the applied force, the lateral distance between the IgM strands increased. The same effects appeared to be different with different proteins. In the case of adsorbed fibrinogen which was scanned with the same applied attractive force of 4nN continuously for 10 minutes, only a minor manipulation of the adsorbed molecules was observed indicating a greater adhesion between this protein and mica than between IgM and mica. With an applied repulsive force of 30 nN, fibrinogen strands finally formed. With this force the adsorbed fibrinogen could be manipulated into different shapes thus allowing us to write protein "letters" and "signs" on the mica surface. At a much higher repulsive force, the entire scanning area was swept clean. Although such experimental artifacts may present a problem in determining the kinetics of protein adsorption to solid surfaces, they may be also useful for making desired ordered arrays of different proteins at interfaces.

Notes :

Abstract, 7th Internat Conf. on Surface & Colloid Science, (July, 1991).

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SYMPOSIUM A2

Nitrate soil testing for adjusting growing-season N fertilizer applications has become possible with the development of colorimetric and ion-specific electrode equipment for in-field measurement of nitrate concentrations. Calibration data for nitrate soil testing in humid regions is limited. Seventeen field experiments were conducted in Virginia in 1990 to develop calibration data for using a nitrate soil test to adjust N fertilizer applications for corn, and to compare three "quick-test" procedures for soil nitrate measurement with standard laboratory techniques. Surface soil textures varied from sandy loam to silty clay loam and soil nitrate contents in the surface 30 cm of soil ranged from 5 to 63 ppm when the corn was 30 cm tall. No preplant N fertilizer was applied and corn responded to side-dress N fertilizer applications (0 to 270 kg N/ha) at 9 locations. Grain yields were excellent at all but one site. No grain yield responses were observed with soil nitrate levels greater than 25 ppm, however, several sites with nitrate levels varying from 10 to 16 ppm also did not respond to N fertilization. Further work is needed to establish a critical soil nitrate level for this type of procedure. The three "quick-test" procedures were highly correlated (r = 0.94, 0.95, and 0.96) with the standard laboratory technique for measuring soil nitrate.

Anticonvulsant Drugs, Folic Acid, and Pregnancy Outcome in Epileptic Women. E. ANDERMANN, L. DANSKY, M. OGUNI, AND D. ROSENBLATT (Departments of Neurology and Neurosurgery, Biology, Pediatrics, Medicine, and The Centre for Human Genetics, McGill University).

Folate deficiency has been postulated as a possible mechanism for the teratogenic effects of anticonvulsant drugs (AED). Serum (SF) and red cell folate (RCF) levels have been shown to be decreased in patients with epilepsy on long term AED treatment. In a prospective study of epileptic women in Montreal, we showed that plasma phenytoin and phenobarbital levels, as well as low blood folate levels prior to and/or early in pregnancy, were significantly correlated with increased risks of spontaneous abortions and developmental anomalies, whereas SF and RCF levels were negatively correlated with plasma phenytoin and phenobarbital levels. The findings suggest a dose-response relationship between AED, folate and adverse pregnancy outcome. Studies assessing the role of periconceptional folic acid-containing vitamin supplementation in reducing the incidence of congenital malformations are controversial. In our study, major congenital malformations were significantly decreased in the past decade, corresponding to a significant increase in mean folate levels in the first trimester.

Night Colony: A Science Discovery Tool. J. D. ANDRADE, J. TOBLER, R. SOFFLETT, T. STODDART, and S. WINTERS (Departments of Bioengineering and Educational Studies, University of Utah).

NIGHT COLONY is a stable, long-lived culture of microalgae, which emit light when mechanically stimulated. Certain marine microalgae, dinoflagellates, are responsible for bioluminescence in oceans, bays, and estuaries. Bioluminescence is a phenomenon which is largely unknown to students and teachers and almost totally excluded from all science curricula and textbooks from kindergarten through college. The NIGHT COLONY device allows the student to discover something completely new. Observation of living light leads immediately to a set of questions. Where does the light come from? Why it blue? Why does one have to tap the container? Why does the light go out? Nearly everyone who discovers and observes bioluminescence is impressed and motivated to see and learn more. How can you have light without batteries, bulbs, or wires. The students, and their teachers, discover their own answers and are led into various areas and aspects of science.

NIGHT COLONY is the first of a series of science education materials and tools which will permit students and teachers to probe into biology, chemistry, physics, geology, and environmental sciences in a process of highly integrated science education. Bioluminescence is not a completely understood phenomenon, it is living, breathing, developing field of science, not an old, established subject. It cannot be treated didactically, it must be treated in an observational and experimental manner and thus is an ideal tool by which to encourage scientific inquiry, discovery, and reasoning.

Acknowledgment: This work has been supported by Protein Solutions, Inc., Salt Lake City.

Multidimensional Theories and Philosophy of Science. ALFREDO ANDRADE-CARRENO (Department of Sociology. University of California Los Angeles. Visiting Scholar. Facultad de Ciencias Políticas y Sociales. Universidad Nacional Autónoma de México. Professor).

The contemporary development of social sciences seems to depend on the efforts to perform new multidimensional theoretical synthesis capable to articulate micro-macro analysis levels of social action.

Jürgen Habermas, in Germany during 1960s, and Jeffrey C. Alexander, in the United States during 1980s, have developed two alternatives to construct this multidimensional synthesis for social sciences, from Functionalism and Critical Theory, respectively. These approaches have as common framework the Functionalist theory of social action created by Talcott Parsons.

In this paper, I analyze the particularities of the philosphy of science that supports each synthetical theory. I conclude that although the main contradictions between these multidimensional theories, they can be viewed as complementary theoretical approaches.

U.S. Forest Service, Intermountain Region, Threatened, Endangered, and Sensitive (TES) Plant Program. Duane Atwood, U.S. Forest Service, Intermountain Region, Ogden, Utah 84401.

An overview of the plant program for Utah, Nevada, Idaho, and portions of Wyoming and California are discussed. A brief history of the program is presented with emphasis on the current program, and the future direction over the next decade. A comparison with other Forest Service regions is made with data presented on budgets, botanical staffing trends and needs within the Forest Service. Federally listed and sensitive plants are discussed.

Amelioration Effects of Calcium Amendments on the Growth of Phaseolus vulgaris L. under Sodium Stress. S.M. AWADA, L. M. DUDLEY, Utah State University.

Two greenhouse experiments were conducted to determine the amelioration effect of Ca salts ($CaCl_2$ and $CaSO_4$) on the growth of snapbeans under Na stress, and to determine the effect of ion speciation on the uptake of Ca, Na, SO_4, and Cl by snapbeans. In experiment 1, the seeds were grown in sand and vermiculite. The treatment solutions were 0, 20, 40, 60, and 80 $mmol_c/L$ NaCl or Na_2SO_4. In experiment 2, the treatment solutions were 0, 15, 30, 45, and 60 $mmol_c/L$ NaCl or Na_2SO_4 combined with $CaSO_4$ or $CaCl_2$ at concentrations of 15 or 30 $mmol_c/L$. At any given concentration, ANOVA showed that NaCl decreased the biomass more than Na_2SO_4. Also NaCl treatment resulted in increased Ca and Na uptake as compared to Na_2SO_4. Sodium uptake was related to the concentrations of complexes species rather than to free Na ion. Whereas, Ca, SO_4, and Cl uptake was correlated to free ion concentrations. The results also showed that the presence of $CaSO_4$, with NaCl or Na_2SO_4, decreased the uptake of Na and Ca ion relative to $CaCl_2$ treatment.

Outdoor Adventures in Discovering Nature: A Blending of Adventure and Environmental Education. L. Ballard (Fisheries and Wildlife Department, Utah State University); S. Ohlhorst (Fisheries and Wildlife Department, Utah State University).

One of the great needs in education today is to develop in future generations an awareness of the natural world and their stewardship over it. This four day course represents an innovative and integrated approach to developing student awareness, appreciation, and knowledge about the complex yet elegant characteristics of the outdoor environment. This course incorporates the two traditional approaches to outdoor education, those of adventure education and environmental education. As the students explore and discover their world four interrelationships among natural resources, people and society are fostered: the interpersonal and intrapersonal (relationships with others and self), important components of adventure education, and the ecosystemic and ekistic (relationships between organisms and their environment and between people and their surroundings), key components of environmental education.

In addition to this unique blending of educational philosophy, this course incorporates an interdisciplinary approach whereby, for example, creative writing and artwork are used to develop skills in creative and critical thinking. Sensory awareness and hands-on activities are

PACIFIC AAAS DIVISION

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Volume 10, Part 1 — June 23, 1991

72ND ANNUAL MEETING OF THE PACIFIC DIVISION, AAAS

PROGRAM WITH ABSTRACTS

AAAS - Pacific Div. 1991
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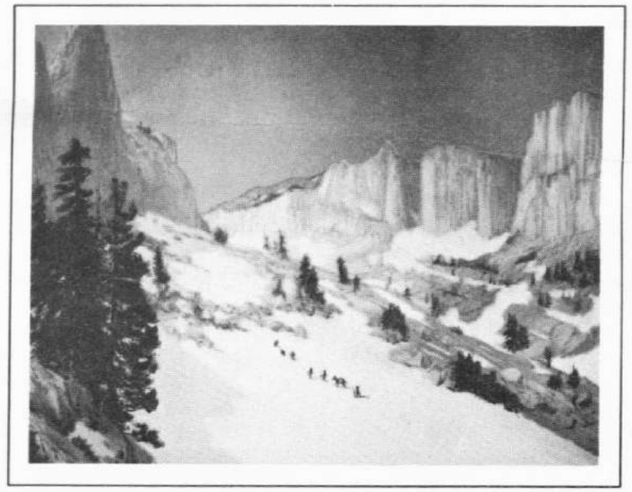


UTAH STATE UNIVERSITY, LOGAN

JUNE 23-27, 1991

Nitrate soil testing for adjusting growing-season N fertilizer applications has become possible with the development of colorimetric and ion-specific electrode equipment for in-field measurement of nitrate concentrations. Calibration data for nitrate soil testing in humid regions is limited. Seventeen field experiments were conducted in Virginia in 1990 to develop calibration data for using a nitrate soil test to adjust N fertilizer applications for corn, and to compare three "quick-test" procedures for soil nitrate measurement with standard laboratory techniques. Surface soil textures varied from sandy loam to silty clay loam and soil nitrate contents in the surface 30 cm of soil ranged from 5 to 63 ppm when the corn was 30 cm tall. No preplant N fertilizer was applied and corn responded to side-dress N fertilizer applications (0 to 270 kg N/ha) at 9 locations. Grain yields were excellent at all but one site. No grain yield responses were observed with soil nitrate levels greater than 25 ppm, however, several sites with nitrate levels varying from 10 to 16 ppm also did not respond to N fertilization. Further work is needed to establish a critical soil nitrate level for this type of procedure. The three "quick-test" procedures were highly correlated (r = 0.94, 0.95, and 0.96) with the standard laboratory technique for measuring soil nitrate.

Anticonvulsant Drugs, Folic Acid, and Pregnancy Outcome in Epileptic Women. E. ANDERMANN, L. DANSKY, M. OGUNI, AND D. ROSENBLATT (Departments of Neurology and Neurosurgery, Biology, Pediatrics, Medicine, and The Centre for Human Genetics, McGill University).

Folate deficiency has been postulated as a possible mechanism for the teratogenic effects of anticonvulsant drugs (AED). Serum (SF) and red cell folate (RCF) levels have been shown to be decreased in patients with epilepsy on long term AED treatment. In a prospective study of epileptic women in Montreal, we showed that plasma phenytoin and phenobarbital levels, as well as low blood folate levels prior to and/or early in pregnancy, were significantly correlated with increased risks of spontaneous abortions and developmental anomalies, whereas SF and RCF levels were negatively correlated with plasma phenytoin and phenobarbital levels. The findings suggest a dose-response relationship between AED, folate and adverse pregnancy outcome. Studies assessing the role of periconceptional folic acid-containing vitamin supplementation in reducing the incidence of congenital malformations are controversial. In our study, major congenital malformations were significantly decreased in the past decade, corresponding to a significant increase in mean folate levels in the first trimester.

Night Colony: A Science Discovery Tool. J. D. ANDRADE, J. TOBLER, R. SOFFLETT, T. STODDART, and S. WINTERS (Departments of Bioengineering and Educational Studies, University of Utah).

NIGHT COLONY is a stable, long-lived culture of microalgae, which emit light when mechanically stimulated. Certain marine microalgae, dinoflagellates, are responsible for bioluminescence in oceans, bays, and estuaries. Bioluminescence is a phenomenon which is largely unknown to students and teachers and almost totally excluded from all science curricula and textbooks from kindergarten through college. The NIGHT COLONY device allows the student to discover something completely new. Observation of living light leads immediately to a set of questions. Where does the light come from? Why it blue? Why does one have to tap the container? Why does the light go out? Nearly everyone who discovers and observes bioluminescence is impressed and motivated to see and learn more. How can you have light without batteries, bulbs, or wires. The students, and their teachers, discover their own answers and are led into various areas and aspects of science.

NIGHT COLONY is the first of a series of science education materials and tools which will permit students and teachers to probe into biology, chemistry, physics, geology, and environmental sciences in a process of highly integrated science education. Bioluminescence is not a completely understood phenomenon, it is living, breathing, developing field of science, not an old, established subject. It cannot be treated didactically, it must be treated in an observational and experimental manner and thus is an ideal tool by which to encourage scientific inquiry, discovery, and reasoning.

Acknowledgment: This work has been supported by Protein Solutions, Inc., Salt Lake City.

Multidimensional Theories and Philosophy of Science. ALFREDO ANDRADE-CARRENO (Department of Sociology. University of California Los Angeles. Visiting Scholar. Facultad de Ciencias Políticas y Sociales. Universidad Nacional Autónoma de México. Professor).

The contemporary development of social sciences seems to depend on the efforts to perform new multidimensional theoretical synthesis capable to articulate micro-macro analysis levels of social action.

Jürgen Habermas, in Germany during 1960s, and Jeffrey C. Alexander, in the United States during 1980s, have developed two alternatives to construct this multidimensional synthesis for social sciences, from Functionalism and Critical Theory, respectively. These approaches have as common framework the Functionalist theory of social action created by Talcott Parsons.

In this paper, I analyze the particularities of the philosphy of science that supports each synthetical theory. I conclude that although the main contradictions between these multidimensional theories, they can be viewed as complementary theoretical approaches.

U.S. Forest Service, Intermountain Region, Threatened, Endangered, and Sensitive (TES) Plant Program. Duane Atwood, U.S. Forest Service, Intermountain Region, Ogden, Utah 84401.

An overview of the plant program for Utah, Nevada, Idaho, and portions of Wyoming and California are discussed. A brief history of the program is presented with emphasis on the current program, and the future direction over the next decade. A comparison with other Forest Service regions is made with data presented on budgets, botanical staffing trends and needs within the Forest Service. Federally listed and sensitive plants are discussed.

Amelioration Effects of Calcium Amendments on the Growth of Phaseolus vulgaris L. under Sodium Stress. S.M. AWADA, L. M. DUDLEY, Utah State University.

Two greenhouse experiments were conducted to determine the amelioration effect of Ca salts ($CaCl_2$ and $CaSO_4$) on the growth of snapbeans under Na stress, and to determine the effect of ion speciation on the uptake of Ca, Na, SO_4, and Cl by snapbeans. In experiment 1, the seeds were grown in sand and vermiculite. The treatment solutions were 0, 20, 40, 60, and 80 $mmol_c/L$ NaCl or Na_2SO_4. In experiment 2, the treatment solutions were 0, 15, 30, 45, and 60 $mmol_c/L$ NaCl or Na_2SO_4 combined with $CaSO_4$ or $CaCl_2$ at concentrations of 15 or 30 $mmol_c/L$. At any given concentration, ANOVA showed that NaCl decreased the biomass more than Na_2SO_4. Also NaCl treatment resulted in increased Ca and Na uptake as compared to Na_2SO_4. Sodium uptake was related to the concentrations of complexes species rather than to free Na ion. Whereas, Ca, SO_4, and Cl uptake was correlated to free ion concentrations. The results also showed that the presence of $CaSO_4$, with NaCl or Na_2SO_4, decreased the uptake of Na and Ca ion relative to $CaCl_2$ treatment.

Outdoor Adventures in Discovering Nature: A Blending of Adventure and Environmental Education. L. Ballard (Fisheries and Wildlife Department, Utah State University); S. Ohlhorst (Fisheries and Wildlife Department, Utah State University).

One of the great needs in education today is to develop in future generations an awareness of the natural world and their stewardship over it. This four day course represents an innovative and integrated approach to developing student awareness, appreciation, and knowledge about the complex yet elegant characteristics of the outdoor environment. This course incorporates the two traditional approaches to outdoor education, those of adventure education and environmental education. As the students explore and discover their world four interrelationships among natural resources, people and society are fostered: the interpersonal and intrapersonal (relationships with others and self), important components of adventure education, and the ecosystemic and ekistic (relationships between organisms and their environment and between people and their surroundings), key components of environmental education.

In addition to this unique blending of educational philosophy, this course incorporates an interdisciplinary approach whereby, for example, creative writing and artwork are used to develop skills in creative and critical thinking. Sensory awareness and hands-on activities are

PACIFIC AAAS DIVISION

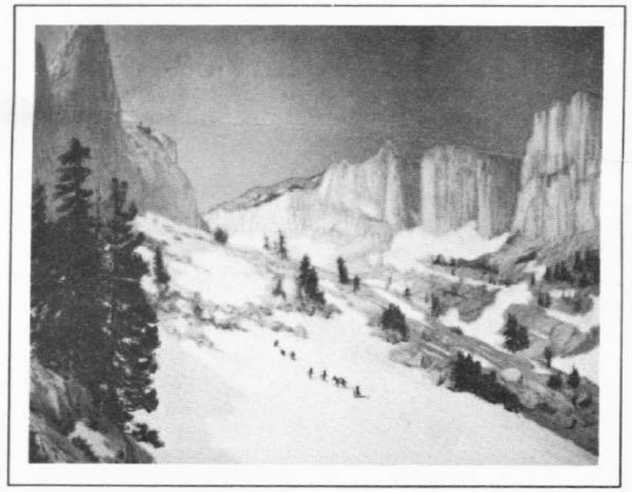
PROCEEDINGS OF THE
PACIFIC DIVISION, AMERICAN ASSOCIATION FOR THE
ADVANCEMENT OF SCIENCE

Volume 10, Part 1 — June 23, 1991

72ND ANNUAL MEETING OF THE PACIFIC DIVISION, AAAS

PROGRAM WITH ABSTRACTS

AAAS - Pacific Div. 1991
USU Logan



UTAH STATE UNIVERSITY, LOGAN

JUNE 23-27, 1991

Annals of
Biomedical Engineering

The Journal of the
Biomedical Engineering Society

19 (5) 1991

Special Issue
for the
1991 Annual Fall Meeting
of the
Biomedical Engineering Society

I.4. *Bioengineering and the Costs of Health Care*

Organizer: Joseph D. Andrade, University of Utah

91-15. "What, Me Worry?" Bioengineering and the Costs of Health Care

J.D. Andrade, University of Utah

The rapidly increasing cost of health care in the United States is now a subject of considerable interest and concern for all segments of society. Historically, the academic bioengineering community has not been particularly concerned with the cost implications of the technologies and instruments which it develops. The medical community, which applies the results of bioengineering research and development, has also been generally unaware and unconcerned with cost considerations until relatively recently. The situation of course has changed dramatically in recent years. It is now imperative that at least a portion of academic bioengineering education, research, and development be directed to the health care cost issue.

The graduates of academic bioengineering programs nationally go on to work in the health care products industry, in government regulatory bodies, and in academia. Students in bioengineering programs should be induced to consider the cost-benefit implications of their graduate research work and should have some general familiarity with the concepts and techniques of technology assessment and cost benefit analysis.

Academic bioengineering should take a global look at primary medical care activities and should create new and novel approaches which could have a significant impact on *decreasing* health care costs. It is not someone else's problem—it is also *our* problem.

91-16. The Changing Environment for Bioengineering

Robert P. Huefner and Joseph Andrade, University of Utah

Our health care delivery and financing systems are going through revolutionary change. The biggest changes are likely to come from some form of national health insurance, probably within the next two decades.

"Access, access" was the call behind most health care reform after World War II, but in 1965 we bit off more than we realized. Within half a decade the twin reforms of Medicare and Medicaid greatly increased the utilization of health care services, and with that brought crisis to state and federal budgets during the Seventies and through the Eighties. The explosion in costs was not limited to government. Utilization and costs of health care also burgeoned for the privately insured and the uninsured. Governments and employers raised a new cry: "cost containment!" They drowned the calls for access—but only temporarily. Cost management and a structurally flawed insurance market today create desperate access problems, especially for small businesses and for individuals with prior medical problems. In the Nineties the health care delivery system fails our expectations on both counts of access and costs, and we wonder if attempts to address these two concerns soon will threaten quality as well.

For the next few years there will be desperate, confused, and sometimes innovative actions at both the state and federal levels. These deserve careful watching and guidance, in part because they will determine the health care system which will form the environment for the future of bioengineering.

The future certainly means the introduction of new levels of cost consciousness in bioengineering. Experimentation with unproven technologies, especially expensive technologies, will be discouraged, as much as they were encouraged in the past. Whether funding for new technologies will be easier or tighter is less certain. What seems reasonably predictable is that the funding sources, whether public or private, will shift their interests to cost-saving technologies. Opportunities here are largely untapped, and appear to be enormous.

91-17. Medical Technology and National Health Care Proposals

William W. Cimino, Department of Bioengineering, University of Utah

The use of "high technology" in the practice of medicine is frequently cited as one reason for the rapidly escalating cost of health care in the United States. At the same time, advancements in medical technology have increased both the quality and capability of available medical care. Thus, technology is directly involved with both the cost and quality issues of medical care, and it seems appropriate that the role of technology would be a central issue in any national health care proposal.

This paper examines the relationship between the use, availability, and development of medical technology and five proposed national health care plans: (1) the Basic Health Benefits for All Americans Act (BHBAAA, the Kennedy-Waxman Bill); (2) the Physicians for a National Health Program proposal (PNHP); (3) the Consumer-Choice Health Plan for the 1990's (CCHP) by Enthoven and Kronick; (4) the National Health System for America (NHSA) proposal from the Heritage Foundation; and (5) the Health Access America (HAA) proposal from the AMA. Each of these plans address health care coverage, plan financing, and cost containment strategies to varying degrees, yet none of the plans specifically address the role of technology, other than to suggest that technology assessment would be required for success of the plan (PNHP and CCHP). However, implementation of any of the plans would have direct and/or indirect effects on the availability, use, and development of medical technology, and hence, the quality and cost of health care under the plan.

91-18. The Oregon Priorities: A Bioengineering Resource

J.D. Andrade and R. Huefner, Departments of Bioengineering and Political Science, The University of Utah

The State of Oregon is leading the nation with an ambitious and important effort to address the health care cost problem (J. Kitzhaber, "A Healthier Approach to Health Care," *Issues in Science & Technology*, Winter 1990–91, pp. 59–65).[1] After a 2-year effort, involving all segments of the Oregon population, Oregonians have categorized and prioritized health care into 17 generic categories and nearly 800 specific procedures. At the top of their priority list are ". . . life-threatening conditions for which treatment will return a person to health; maternity services; preventive care for children such as screening and diagnosis; and preventive care for adults." At the bottom are ". . . treatments which will marginally improve a person's quality of life although they may not prolong it." (Oregon Basic Health Services Program Report, April, 1991, Dept. of Human Resources, Office of Medical Assistance Programs, State of Oregon, Salem, Oregon).[2] The data they have collected and the assessments and prioritization they have developed can serve as a resource for bioengineering researchers and developers in their choice of cost-effective projects and studies. We review the Oregon categories and suggest areas where academic bioengineering activities could have an important influence on decreasing the costs of health care.

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BMES Abstract

Using Bioengineering for Science Education

J.D. Andrade
Department of Bioengineering, 2480 MEB
Salt Lake City, Utah 84112

There is growing interest in enhancing science and technical education at all levels in our society and particularly for the general public.

Among the greatest motivators of our population are the topics of sports, sex, and health. All three of these natural motivators are directly related to bioengineering. The general public in science museums and science centers and students in schools are highly motivated by experiments which involve their own body. It is clear that simple, safe measurements of a variety of physiological functions can be used as motivators and as sources by which to develop science and technical education concepts.

A group of bioengineering graduate students enrolled in a special projects course to develop and apply physiologic measurements, made very simply, inexpensively and safely, to demonstrate and develop a variety of science and technical principles and applications.

Simple measurements and experiments were used as a vehicle to develop a wide range of science concepts and skills of increasing levels of depth and sophistication.

Abstract

Closed Ecosystems as Tools for Integrated Science Education

by J.D. Andrade, Ph.D.

Proteins Solutions Inc.,
Salt Lake City, Utah, and
The University of Utah,
Center for Integrated Science Education

It is important that teachers, students and the general public be made aware of the close connection between NASA's interests and objectives on life support of man in space and the parallel problems of maintenance and enhancement of a hospitable terrestrial environment for man. The development and availability of materially closed ecosystems, and particularly bioluminescent ones, as research and education tools could significantly enhance the general public's awareness of the importance of NASA's objectives and mission.

In addition, the availability of such ecosystems could greatly enhance science education at the elementary, junior high, and high school levels, and thereby contribute significantly to improving science education in this nation.

We have demonstrated that the use of *bioluminescence* in particular provides a highly motivational and novel approach to integrated science education. Using commercially available kits and related materials the instructor or parent can utilize this interesting biological process to teach the fundamentals of biology, as well as many fundamentals of chemistry, physics, and earth science. Examples and demonstrations will be provided.

Address:

J.D. Andrade
Protein Solutions, Inc.
6009 Highland Drive
Salt Lake City, Utah 84121
(801) 277-1259

Andrade 1992
Discussion at

The Utah International Medical Device Congress

Competitiveness in Medical manufacturing

Held February 12-14, 1992
Salt Lake City, Utah

Editors:
Ross E. Robson
Frederick M. Huchel
Glenn D. Morris

Office of Business Relations
College of Business
Utah State University

Published by:
The Shingo Prize
for Excellence in
American Manufacturing

and
State of Utah Biomedical
Industry Council

Joseph Andrade

I have enjoyed the meetings very much. I would like to make three brief points. As one who has been working for the past 25 years in bio-materials and bio-compatibility, I was pleased with Commissioner Kessler's new emphasis on science within the agency. The bio-materials initiative within the FDA is probably going to be very helpful and very useful to the entire industry as well as to the agency. It is also important to note that the National Institutes of Health (NIH) are now involved in a strategic planning exercise, just as the FDA is apparently involved in a strategic planning exercise. I was in a meeting yesterday in Los Angeles, the first of four regional, public meetings to provide input to the National Institute of Health regarding strategic planning. Medical devices, bio-engineering, and bio-materials have never been a major part of NIH's interests or emphasis. It is likely that it is going to change, at least somewhat. The new NIH strategic plan draft does include a significant component in the area of bio-technology, bio-engineering, and bio-materials. My hope is that the FDA and the NIH will begin to talk to one another about these issues. Apparently, there hasn't been all that much interaction in the past.

I would also like to say a word about science because I think there is a great misconception of what science is and what it can do in this field as well as many other fields. You heard in Commissioner Kessler's remarks a continuous emphasis on "science," "science-based," and science this and science that, as if science had any black-and-white answers on safety and effectiveness. Science has no black-and-white answers. There are very few areas of science without controversy. I think that needs to be understood by the regulators, certainly by the lawyers, and certainly by the media. The media looks to "yes" or "no" answers, "black" and "white" answers from science. Science is full of controversy. The best that science can do is give you probability figures. It is all based on statistics. When we say something is safe and effective, we can't say that in an absolute sense. It is like Environmental Protection Agency (EPA) talking about zero levels of some chemical. There are no zero levels of anything. Everything is out there; it is a question of how sensitive you want to measure it. It is the same with safety and effectiveness. It is all relative; it depends on the device; it depends on the application; it depends on the costs; it depends on the cost-benefit assessment and a benefit-risk assessment.

My final point is—and I don't always agree a lot with Senator Hatch, but in this case I agree with one of his points—that we all have the responsibility to inform and to educate, we as academics, we as industry folks, and we as regulators and government agency folks. The general public, the general patient, regulators, your typical lawyer, and almost everyone else out in the community doesn't understand that there are no absolutes. You can't just say a device is safe. It is safe for some proportion of use, for some particular area, under certain sets of conditions. Nothing is safe; life is inherently dangerous. We are all going to die eventually, with or without a medical device. So it is our responsibility to educate the media, to educate our lawyer friends, to educate

our regulator friends, and to educate ourselves that you can't use science as a total crutch. We have to simply be honest and open and give some statistics and some numbers. I have enough faith in the general population of this country that if they are given the facts objectively as to what the risks are with the device, what the potential benefits are of that device, and the costs of that device, they can then choose. The only way we can do that is for everyone involved in the equation to be completely honest, open, and objective, and know something about statistics.

Nancy Taylor

Our next speaker is William Appler, who is in private practice. He will discuss David Kessler's announcement of the Re-Assessment of Information on Safety and Effectiveness Program (RAISE).

William Appler

I am not sure how I always manage to get scheduled as the only thing between the audience and lunch. But as you sit out there and listen to the things we have to say, we hope you will think of questions and send them up so we can respond to them. In part, to help stimulate you on that, I want to call my topic today, "An Educated No."

In any personal or professional relationship we have, we have to have the ability to say "no." It is not pleasant to say "no" to our children, our spouses, our friends, or our colleagues, but it is sometimes necessary. My suggestion to you today is the medical device industry all too infrequently is saying "no" to FDA. It is true we are a regulated industry. We are under the FDA gun. We are certainly becoming more regulated. From the Safety Medical Device Act (SMDA), to dura tracking, to the RAISE Program I will talk about briefly today, what you have seen in the past really seems to be nothing like what you are going to see in the future. But the question still remains open to individual companies; "Who is going to regulate us?" "Are we going to regulate ourselves?" "Are consultants and others we hire going to regulate us?" or, "Is the FDA going to regulate us?" "Who is going to have that final word?" My suggestion to you is that we should have the final word. Now that takes some expenditures, resources, time, personnel, and so forth. But you have to stay on top of these regulations, so that when FDA comes in, you will know as much about their regulations as you do about your company. Isn't it fairly ridiculous that perhaps after 10 or 15 years of making a product, somebody, who has not been trained in your field and might spend most of his time inspecting food companies, is going to come in and tell you how to run it? What the company has to do is know more than that investigator so that you can say "no" to the FDA. I have talked to a lot of companies who are hesitant to say that because they think there will be retaliation, approvals won't go through, 10 inspectors will come next time, and so forth. Well, after almost 20 years of doing this, I have never seen the FDA retaliate. There may have been some instances; I am not saying there have been none. I'm just saying that I have said "no" an awful lot of times, and I have never seen a company treated poorly for telling the FDA, "No, we think you

evidence out there to believe that a device's quality, efficacy, and effectiveness can be significantly improved, then I think it is in everybody's best interest to try to do that. That is what competitiveness is all about. You can't mandate that; you can't legislate that; you can't regulate that too directly unless safety is involved.

William Appler

I think another thing that is very important is the ability to have some understanding of what the standards are around the world. Since most of us are involved in global activity, global business, we would like the regulatory agencies of the world to have some concept of what a level playing field would be. It is one of the reasons that we certainly supported activities within ISO to try to have some understanding of truly good, workable, international standards so that we all know in advance what the rules ought to be and know how to play. Certainly, it encourages us to try to get more activity by the FDA to be working with ISO and with the other regulatory agencies in the U.K., France, Germany, Japan, etc.

Nancy Taylor

This next question is directed to the Commissioner but will be a good question for this panel. It references Commissioner Kessler's direct relationship in examination of the small device manufacturer and the approval for new drugs. Small companies who are truly dedicated to both regulatory compliance and product excellence may not be financially capable of completing clinical trials similar to those of the drug industry. So how will small business survive in the scientific support data era?

Robert Rylee

I will make a comment; I am certainly not smart enough to have an answer. Obviously, this is going to put a tremendous amount of pressure on the small companies that do have very limited financial resources to meet the ever increasing demands of the agency. This is particularly true when the agency makes each company go back and document a lot of things that, in reality, are already out there in the public domain. But in support of your application, you have to start at ground zero and re-do a lot of these tests and so on. I think that is a very, very serious issue, particularly for the smaller companies; but it will add costs to everybody.

Joseph Andrade

Related to that, I think, is the issue of where NIH might play a rôle in all of this. NIH has as part of its mission clinically related research. That basically means testing of drugs, procedures, and devices in its clinical research centers. Historically, there has not been a lot of that done with medical devices. That is what I alluded to earlier that the FDA and NIH need to get together. They are both in the process of formulating strategic plans. There has to be some small overlap in those new plans to be sure that those agencies interact effectively.

making, and then go see Bob Sheridan, David West, and the head of General Hospital's personal products division. Give them the opportunity to do something about it, then, as Howard suggests, go see Amanda Pedersen[3] who is the ombudsman, and has been there for some 15 months. She is not exactly overwhelmed with things to do. You better expect to go through the process. You might also make some judgements as to how you can live with the results of the process. If it is completely unlivable, then you've got to either get the FDA to change it or find some other solution. I have every reason to believe the woman will be very open-minded toward these kinds of suggestions. An ombudsman who never corrects anything doesn't build much of a reputation.

Nancy Taylor

I am going to take my moderator's cap off and ask my own question. It is one that is similar to one that was asked.

I think that today what a lot of us inside Washington and out of Washington are feeling is this real conflict in competing with the FDA versus industry. Commissioner Kessler is living up to his nickname of Elliott Ness. Tension builds when there is a lot of conflict and deep interpretation of the law. I would like to ask each panel member if they were to take David Kessler aside for five minutes and suggest two things that he could do better in terms of enhancing coöperation and in building support for his effort in the FDA, what would they tell him?

Joseph Andrade

It is an interesting question. We were discussing this in the hall just a few minutes ago. One possibility is to bring into the FDA people with strong medical device industry experience for short periods of time, perhaps a two year stint; many other federal agencies do that. They recruit people to actually work and manage their programs for short periods of time. It gets away from the beltway mentality and infuses fresh ideas, and fresh blood from the real world beyond the beltway. These people, after their one or two year stint, go back. There are some potential conflict of interest issues but they can be managed. It is done in the Department of Defense. It is done, I think to some extent, in the EPA. It is done in other government agencies. It is a possibility.

(Unknown Speaker)[4]

I can think of two or three things. Number one, I certainly agree with what you have said. I think the agency has to have more people who are truly expert in the various themes of technology in which they are expected to do things. That is a good way to put it. I think, obviously, there needs to be more in the way of truly up front dialogue with industry. The FDA recently has started working in, what I would call, almost a vacuum. I go back many years in the orthopedic implant industry when we did have on-going dialogues with the FDA. Things worked a whole lot better. We knew what they were thinking about, what their expectation was, and we were able to accommodate that. Recently, that is not the way things have been happening. The FDA will not have

Abstract

AIMBE Conference
Medical and Biological Engineering:
A Celebration of the Past and Challenges of the Future
February 24-25, 1992
Washington, D.C. 20418

Bioengineering and the Costs of Health Care

J.D. Andrade, Professor
Department of Bioengineering
University of Utah
Salt Lake City, Utah 84112

The rapidly increasing cost of health care in the United States is now a subject of considerable interest and concern for all segments of society. Historically, the academic bioengineering community has not been particularly concerned with the cost implications of the technologies and instruments which it develops. The medical community, which applies the results of bioengineering research and development, has also been generally unaware and unconcerned with cost considerations until relatively recently. The situation of course has changed dramatically in recent years. It is now imperative that at least a portion of academic bioengineering education, research, and development be directed to the health care cost issue.

The State of Oregon is leading the nation with an ambitious and important effort to address the health care cost problem (J. Kitzhaber, "A Healthier Approach to Health Care," Issues in Science & Technology, Winter 1990-91, pp. 59-65). After a 2-year effort, involving all segments of the Oregon population, Oregonians have categorized and prioritized health care into 17 generic categories and nearly 800 specific procedures. At the top of their priority list are "...life-threatening conditions for which treatment will return a person to health; maternity services; preventive care for children such as screening and diagnosis; and preventive care for adults." At the bottom are "...treatments which will marginally improve a person's quality of life although they may not prolong it." (Oregon Basic Health Services Program Report, April, 1991, Dept. of Human Resources, Office of Medical Assistance Programs, State of Oregon, Salem, Oregon). The data they have collected and the assessments and prioritization they have developed can serve as a resource for bioengineering researchers and developers in their choice of cost-effective projects and studies.

The future certainly means the introduction of new levels of cost consciousness in bioengineering. Experimentation with unproven technologies, especially expensive technologies, will probably be discouraged. Whether funding for new technologies will be easier or tighter is less certain. What seems reasonably predictable is that the funding sources, whether they are public or private, will shift their interests to cost-saving technologies. Opportunities here are largely untapped, and appear to be enormous.

ABST – 22
ANDR

All Polymers are "Intelligent": Polymer Surface Dynamics

J.D. Andrade (Professor of Bioengineering and Materials Science, University of Utah, 2480 MEB, Salt Lake City, UT 84112, USA; (801) 581-4379)

The "intelligence" of synthetic macro-molecules is currently a topic of great interest, popularity, and activity. The understanding of macro molecule mechanics and dynamics has reached the stage where unique and novel applications are being developed.

Basic polymer physicists and material scientists are well aware of the dynamics, the relaxations, and the multitude of conformational states which exist in most polymeric materials. Indeed, it is these very properties that are largely responsible for the unique set of physical and mechanical characteristics which have made polymer materials and the products derived from them so ubiquitous in every day life.

Biopolymers, and particularly proteins and polynucleic acids, have a history, long track record and even expectation of "intelligence." Multiple conformational states, conformational flexibility, cooperativity, specific binding interactions, temperature and pH sensitivities, and a myriad of other properties are all common or expected with biopolymers, yet it is only recently that the same set of expectations has been extended to and attributed to synthetic macro molecules. This is largely because the two worlds have not overlapped in terms of the practitioners.

Fortunately, that situation has changed dramatically in the last decade. The proliferation of programs and research groups in biomedical materials, drug delivery systems, medical devices, and biotechnology has produced hybrid scientists and engineers and their students and co-workers who now expect synthetic macro molecules capable of far more than is normally reflected in polymer materials textbooks.

My focus is on the "intelligence" of surfaces and interfaces, particularly those involving polymers. Surfaces and interfaces operate with the same set of thermodynamic and kinetic rules as do bulk phases. Indeed, the equations of surface thermodynamics are exactly the same as those of bulk thermodynamics with the exception that the interfacial work and interfacial free energy terms are included, rather than neglected as in the case of infinite bulk phase systems. As soon as this is understood, then of course the "intelligence" of polymer surfaces becomes much less of a mystery. Surfaces and interfaces respond to their environments just as do bulk polymers. Surface and interface properties are time and temperature sensitive, as are bulk polymers.

The dynamics of polymer surfaces is well known in the adhesives and textile fiber communities. Indeed, there is a rich patent literature which goes back over 40 years. However, because of the normal classical assumptions of surface chemistry and physics, i.e. that surfaces are homogeneous, flat, rigid, and immobile, the dynamic

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Australia

aspects of most polymer systems has been largely overlooked, ignored, and even unknown to the academic polymer science and surface science communities, until perhaps 20-30 years ago.

About 20 years ago, surface dynamics was rediscovered by the medical devices community, largely through studies on contact lenses. Since then, there has been growing interest and application of polymer surface dynamics in medical and biomaterials problems.

In this lecture I present the basic principles of polymer surface science, basic principles of bulk polymer dynamics, and some selected areas of research and development in polymer surface dynamics.

I conclude with a brief treatment of the complexity of highly dynamic, multi-domain, macro-molecular surfaces and their interactions with highly dynamic multi-domain pseudo-block copolymer proteins and other biomolecules important in biocompatibility and biotechnology.

General references:

1. J.D. Andrade, ed., Polymer Surface Dynamics, Plenum Press, 1987.

WORLD CONGRESS ON MEDICAL PHYSICS AND BIOMEDICAL ENGINEERING
Abstract Form

HEALTH CARE, TECHNOLOGY ASSESSMENT, AND BIOLOGICAL ENGINEERING EDUCATION

J.D. Andrade
Department of Bioengineering, 2480 MEB, University of Utah
Salt Lake City, Utah 84112, U.S.A.

Historically the academic bioengineering community has not been particularly concerned with the costs implications of the technologies and instruments which it develops. The medical community which applies the results of bioengineering research and development has also been generally unaware and unconcerned of cost considerations. Those days are clearly over.

It is now imperative that at least a portion of academic bioengineering education, research, and development be directed to the health care cost issue. The graduates of academic bioengineering programs go on to work in the health care products industry, in government regulatory bodies, and in academia. Students in bioengineering programs should be induced to consider the cost benefit implications of their graduate research work and should have some general familiarity with the concepts and techniques of technology assessment and cost benefit analysis. Academic bioengineering must begin to take a global look at primary medical care activities and should create new and novel approaches which could have a significant impact on decreasing health care costs.

Medical and Biological Engineering in the Future of Health Care is the subject of a recent meeting and the title of a recent volume(1) devoted to these topics and can serve as an appropriate text or discussion document in engineering curricula. The book contains perspectives on medical technology and health care, the key economics and management issues, the role of incentives and new programs, the important role which information and communication technologies can play in alleviating the problem, discusses developments in minimally invasive surgery and diagnostics, considers the role of patients in treatment decisions, and related topics. Such discussions should be, and are expected to become, an important part of all undergraduate and graduate biomedical engineering curricula.

(1) J.D. Andrade, ed., *Medical and Biological Engineering in the Future of Health Care*, University of Utah Press, 1994.

Read INSTRUCTIONS FOR PREPARATION OF ABSTRACTS (page 17) carefully before typing.

If my abstract is accepted, I will attend the World Congress Rio'94 for presentation.

Signature of presenting Author: J.D. Andrade Date: 1/24/94

ABSTRACT Nº: _____
For use of Secretariat only

DEADLINE: DECEMBER 20, 1993

IMPORTANT INFORMATION:

1. Indicate the topic and the subtopic of your paper (SEE THE LIST ON PAGES 12 TO 15):

	TOPIC	SUBTOPIC
1st choice	37	
2nd choice		

2. Preference for presentation (final decision will be made by the scientific committee):
   1. [✓] Oral session
   2. [ ] Poster session
   3. [ ] Either oral or poster session
   4. [ ] Young Investigator Award
   5. [ ] Latin American Student Competition
3. Organizational Affiliations:
   1. [ ] IFMBE
   2. [ ] IOMP
   3. [ ] Other: .....
4. Keywords for indexing:
   1. Technology Assessment
   2. Education
   3. Engineering
5. Authors' names and initials, in the form desirable for alphabetical indexing:
   1. ANDRADE J.D.
   2. .....
   3. .....
   4. .....
   5. .....
   6. .....
   7. .....
   8. .....

Portugal (21)

ENHANCING BIOMATERIALS/BIOENGINEERING COMMUNICATIONS

J.D. Andrade* and K.W. Horch
Dept. of Bioengineering, 2480 MEB, Univ. of Utah, SLC, UT 84112

Introduction

Bioengineers and biomaterials engineers must be able to communicate and interact with a wide range of disciplines and publics. It is therefore essential that they have good communication and presentation skills. Historically, undergraduate science and engineering programs, at least in the United States, have not been very effective at fostering and enhancing communication skills of their students and graduates. This is not dramatically improved in most graduate programs, nor in medical school. Students are generally taught to communicate with peers and/or experts and often have great difficulty communicating with people outside of their field or discipline, and even greater difficulty in communicating with the media or with the general public. This has led to many misunderstandings, misrepresentations, and often a high discomfort level among those involved.

Methods

Several years ago we initiated a scientific presentations course for all students.

This two quarter, 20 week course, at one hour per week, covers a range of topics and issues. During the first quarter the students are exposed to the nature of science and the scientific process, ethics, authorship, and many related issues based in part on the National Academy of Science's publication *On Being a Scientist* [1].

The students choose a topic related to bioengineering. In most cases students have had some research or other technical background which can serve as material for such presentations. In a few cases the students who are already involved in their research utilize such subjects in their presentation. They prepare a formal extended abstract. The abstract is available to the student and faculty audience, and the abstract and the presentation are critiqued with respect to scientific and technical content, and quality of presentation.

Each individual presentation is organized to have a speaker, a formal discussant who acquaints him/herself with the topic and provides a brief formal critique or discussion immediately after the presentation, and a video person who is responsible for slides, overheads, and videotape equipment.

At this stage in their careers we focus primarily on the quality and clarity of the presentation, including the use of effective slides, transparencies, videos, and direct demonstrations of hardware and experiments. They are encouraged to assume that their audience is heterogeneous and consists of peers, experts, and the lay public, such as reporters. The students must participate in the critique of the presentations of all of their fellow students.

They also prepare a separate poster for a departmental and College of Engineering poster contest, which happens to coincide with National Engineers Week in the United States. The posters are prepared according to standard guidelines. The students present and defend their posters to their classmates and faculty and the posters are judged by an outside group. Cash prizes are awarded.

The second quarter of the course, called Controversial Topics in Bioengineering, involves two person debate teams on controversial topics. Table 1 lists the set of topics which were used last Spring. These were intended to be provocative. They are advertised on campus and often draw individuals from other parts of campus, and even the local media. The students are told that they must take sides on the issue -- pro or con, and develop their presentations accordingly.

Table 1.

Topic:
Tissue Engineered Materials Will Replace All Conventional Synthetic Materials
PEO Surfaces are not Blood Compatible
Radial Keratotomy Should be Banned
Low Frequency EM Fields Have Detrimental Bioeffects
Cochlear Implants Do Not Aid the Deaf
Drug Efficacy/Safety Can Now be Determined Without the Need for Animal or Preclinical Studies
Silicone Breast Implants Should be Banned
Implants Cause Cancer -- Eventually
Implanted Electrodes for Brain Stimulation Should be Banned
Prozac is a Dangerous Drug

Results

A growing interest in effective scientific and technical communications among our faculty and students has made this course a success. In fact, we are now finding writing and presentation requirements in most of our core courses. The students generally like the course. Our students are encouraged, even in their first year, to begin to participate in regional and national meetings and conferences as their research topics become formulated and their research activities develop. So the experience in this course is of major benefit to them and they see its relevance in the very near term.

The ability to debate or to take a side, to deal with counter-arguments, opposing views, and to deal with controversial topics, is essential not only in being effective bioengineers and biomaterials scientists, but in being effective and responsible citizens.

Conclusions

Scientists and engineers, in particular, have skills and expertise which are often not available in many public debate or controversial topics. It is essential that we encourage our students, and their faculty, to be involved as responsible citizens in dealing with such issues and controversies.

References

[1] *On Being a Scientist*, National Academy Press, 1989, Washington, D.C.

Kimberly-Clark Abstract; Jan. 21, 2003

Your Private Biochemical Individuality – Development of ChemChips for Metabolome Measurement and Management

J D Andrade, Professor of Bioengineering, Pharmaceutics, and
Materials Science, Univ. of Utah, Salt Lake City

The Genome codes the Proteome; the output of much of the Proteome is the Metabolome. We each have a personal, private Metabolome – a biochemical individuality.

Significant alterations in biochemical processes result in various pathologies or diseases, many of which can be treated by a form of metabolic engineering: controlling or modulating intake of essential nutrients and/or drugs. With the exception of diabetics who regularly monitor glucose, there is little knowledge of the biochemical concentrations of most individuals. The measurements are not generally made because making such measurements requires blood sampling by trained personnel, blood analyses by specialized clinical chemistry laboratories, and professional data interpretation by trained physicians.

We are working to enable care givers, patients, and even healthy individuals to measure up to 50 analytes in a few microliters of minimally invasively derived blood and/or other bio-fluids conveniently, inexpensively, and reliably.

The analytical system includes:

? a ChemChip-- which will include 50 analyte channels requiring initially 100, and later less than 10, microliters of sample;
??ChemWare – substrate-specific enzyme reactions coupled to luciferases to provide sensitive, specific bioluminescence analyses;
? a handheld, portable luminometer, comparable in size and cost to present day glucometers;
??InfoWare—a multi-analyte, multi-axes data presentation and correlation system to provide an icon-like visualization of the information.

Criteria for analyte selection, the identification and selection of specific enzyme reactions for analyte measurement (ChemWare), the simulation and laboratory evaluation of the analytical process, and the drying and implementation of the assay on the ChemChip device will all be discussed.

Progress to date on the various components of our Metabolome Measurement System (MMS) will be discussed, with emphasis on its application to the

metabolic diseases phenylketonuria (PKU) and galactosemia.

The research group includes D Bartholomeusz, R Davies, H Feng, G Yang, S Kern, J Janatova, J Hatch, and several undergraduate students.

Joseph Andrade, Dist. Professor.
Dept. of Bioengineering
University of Utah
50 So Central Campus Center Dr., Rm. 2480 MEB,
Salt Lake City, UT 84112-9202
home: 801-484-4904; cell: 801-706-6747; U of Utah office: 801-581-4379
joeandrade@uofu.net www.utahsciencecenter.org www.bioen.utah.edu/faculty/jda

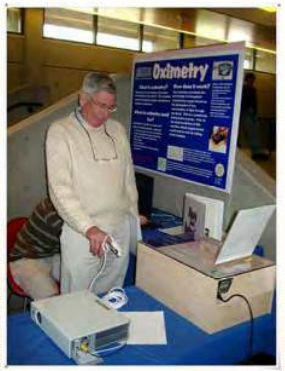
Interactive Exhibits and Programs for the General Public via a Modern Science Center

Joseph Andrade*, Seung-Jae Kim, Michael Anderson, Bioengineering, University of Utah, Salt Lake City, UT.

INTERACTIVE EXHIBITS

The Utah Science Center (USC) opens in 2008 as part of The Leonardo— on Library Square in Salt Lake City. USC will be the first science center to take interactivity and personal involvement to an entirely new level. Targeted to all who will respond to being treated as adults, USC will involve and empower its visitors to be participants – helping to enhance its exhibits and improve its programs. You are more than a visitor – you are more than a participant; you will help create, enhance, and design the experience.

The Utah Science Center emphasizes creative and active exploration of the worlds of science and technology. Visitors to the Utah Science Center will question, learn and invent through personal, hands-on experimentation and exploration. The goal is to facilitate personal Eureka! moments – personal scientific revelations.



DEVELOPMENTS

The Utah Science Center utilizes exhibits and related activities designed, developed, and tested by University of Utah students involved in course projects, thesis projects, and as volunteers.

Students and faculty from

- Architecture and Planning
- Bioengineering,
- Chemistry,
- Geography,
- Geology,
- Materials Science,
- Mechanical Engineering,
- Meteorology,
- Pharmaceutics,
- Physics,

have been involved to date--with additional Departments and programs becoming involved.

Project types have included

- freshman undergraduate laboratory course team projects,
- individual independent project courses,
- Masters degree level thesis projects, and
- high school interns.

SOME OF THE PROJECTS

Active:
- YOU are the Experiment!--the Bioengineering Team
- The Body Electric--more Bioengineers;
- Weather in the West--the Meteorology Team

Developing Projects:
- Chemistry and Chemicals: sophomore organic chemists
- Raging Hormones--Pharmaceutics Team
- Flight!--Mechanical Engineering Team
- PlanetPlace--the Geography Team

SERVICE LEARNING CREDIT

Although some of the activity has been documented and 'blessed' as service learning--much of the work and involvement has not received any formal 'service learning' credit or recognition. The 'credit' or 'recognition' comes in the participants seeing their work used in a public facility committed to science and technical awareness, education, and literacy.

These activities are planned to continue, to expand to many other departments and programs, and to involve greater numbers of students and faculty.

For more details on these activities;
www.utahsciencecenter.org
www.theleonardo.org
(or email to*) **joeandrade@uofu.net**

Society For Risk Analysis Annual Meeting 2007

Risk 007: Agents of Analysis

Session Schedule & Abstracts

** Disclaimer: All presentations represent the views of the authors, and not the organizations that support their research. Please apply the standard disclaimer that any opinions, findings, and conclusions or recommendations in abstracts, posters, and presentations at the meeting are those of the authors and do not necessarily reflect the views of any other organization or agency. Meeting attendees and authors should be aware that this disclaimer is intended to apply to all abstracts contained in this document. Authors who wish to emphasize this disclaimer should do so in their presentation or poster. In an effort to make the abstracts as concise as possible and easy for meeting participants to read, the abstracts have been formatted such that they exclude references to papers, affiliations, and/or funding sources. Authors who wish to provide attendees with this information should do so in their presentation or poster.*

Common abbreviations

W3-F
Choice and Chance: Engaging the Public

Room: 206A 2:00 - 3:30 PM

Chair(s): Joseph Andrade

W3-F.1 14:00 Choice and Chance at The Leonardo--the visitor as participant. ***andrade, Joseph J*; Utah Science Center*** joeandrade@sisna.com

Abstract: **There is a great need in improving the awareness and education of the general public in Risk, Choice, Chance, Decision-making and allied areas. Risk 'communication' must go far beyond traditional communication tools and strategies to motivate, empower and facilitate effective public awareness, education, and understanding. Decision Place and the Center for the Big Picture aremajor components of The Leonardo and the Utah Science Center--opening 2009 in Salt Lake City. Novel plans and developments for The Leonardo include: Miracles Happen! (1 in a Million) Unknown or Unknowable? From Simple games to Chess—and Beyond Numbing of Large Numbers Story, Narrative, Emotions, and Individuals Each of these areas will be briefly described and activities demonstrated.**

SRA participants will be urged to contribute ideas and perspectives.

W3-F.2 14:30 From Research to Public Awareness and Education. ***Slovic P*, Walter C; University of Oregon*** pslovic@pop.uoregon.edu

Abstract: **This discussion will focus on public awareness and involvement via a modern, interactive science exhibit--Risk! Risk! is an interactive, multi-dimensional traveling exhibit developed by the Fort Worth Museum of Science and History that examines risk and risk assessment: how risk affects our lives, how we view risk and why, and how we can better understand and deal with risk using science, mathematics, and critical thinking skills. The research foundation for Risk! and the process of developing and testing the exhibit will be discussed. SRA members will be encouraged to provide input.**

W3-F.3 15:00 Risk, humor, and the SRA. ***Thompson KM*; Harvard School of Public Health*** kimt@hsph.harvard.edu

Abstract: **Popularity of risk analysis as a profession continues to grow and understanding risk represents an essential skill given an increasing number of main-stream media dedicating space to covering risk. Nonetheless, most students do not study risk as a subject as part of their pre-college education and many people would benefit from more basic training related to dealing with risk. This talk will discuss the use of humor and games as powerful tools for engaging people to think about risk and risk-related concepts. The talk will also explore opportunities for the SRA and its members to get more involved in risk education, potentially through supporting efforts to develop curricula and exhibits. Most of this session will involve responding to questions from session attendees and interactive dialogue.**

[back to schedule]

Bioengineering Education via Projects and Activities for an Interactive Science Center: the University of Utah Experience

Joseph Andrade*, Seung-Jae Kim*, Douglas A Christensen
Dept. of Bioengineering, University of Utah, Salt Lake City, UT 84112 and
*The Leonardo, 210 East 400 South, Ste. 14, Salt Lake City, UT 84111

www.bioen.utah.edu

www.theleonardo.org

The Public

A functioning democracy requires a literate, aware, educated, involved, and responsible electorate. Because the general public is very interested in bioengineering and medical technologies, these subjects provide an avenue for enhanced and expanded activities related to scientific and technical literacy.

The Science Center

Science Centers provide opportunities for the general public to experience, participate, and learn a wide range of science and engineering fields. Most major urban areas have a science and technology center—see www.astc.org

The Leonardo -- opening in 2010 in Salt Lake City as a major center for science, art, and culture—takes interactivity and personal involvement to an entirely new level—using measurements and activities designed and developed by Bioengineering and by other students.

The University

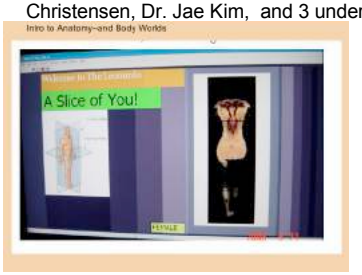
The University's research and education mission extends to its general public and community. Most Universities have 'outreach' and related programs with which to involve, inform, and educate the greater community. Service learning and related community involvement activities are generally fostered and encouraged.

University of Utah programs already involved with The Leonardo include:

Bioengineering	Biology	Chemistry	Geography
Informatics	Meteorology	Pharmacy	Physics

Projects, Exhibits, and People:

A Slice of You?!--a proximity sensor-based human anatomy sectioning experience using the NIH's Visible Human data sets; developed by Prof. D. Christensen, Dr. Jae Kim, and 3 undergraduate students.



Projects, Exhibits, and People:

Is it REALLY Diamond!--Molecular Fingerprinting via fiber optic Raman spectroscopy (unit donated by Process Instruments, Salt Lake City), implemented by summer BioE intern T. Bird and by Drs. J Kim and J Andrade.

Seeing YOUR Insides—personal blood vessel visualization using Bard Access' Site-Rite system (Salt Lake City); implemented by summer intern Alex dePoix and J Andrade.

Private Statistics —a dynamic statistical histogram activity using weight and height sensors; developed by J Abernathy, D Bartholomeusz, Y Al-Sheikh, and J Kim.

Balance Plate —an interactive, competitive balance activity using a Neurocom Balance System (Clackamas, OR); implemented by J Kim and Neurocom.

Bioengineering Students

Bioengineering students have access to undergraduate and/or graduate courses which provide opportunities and environments to design, implement, and test interactive exhibits for a general public audience. The successful exhibits are implemented in ongoing and future programs and activities, such as:
http://www.utahsciencecenter.org/lows/

Current suitable courses at the University of Utah include:
BioE 1102: Intro to Bioeng II (freshman team semester projects)
BioE 5020: Interactive Science Exhibits (independent projects)
BioE 6060/1: Scientific Presentations (beyond PowerPoint!)
BioE 6920: Internship Program

Bioengineering Profession

Bioengineering is a subject of great interest to the general population—as all individuals are involved in various and personal ways with medical technologies, the health care system, etc.; bioengineering, biotechnology, and related topics are among the most popular science/technical topics in magazines, newspapers, and other media. Such intrinsic interest provides an opportunity to involve and educate the public about the field and the profession.

AIMBE (www.aimbe.org) has recognized the potential for encouraging interactions and cooperation between academic bioengineering departments/programs and their local science centers or museums. AIMBE, University of Utah, and The Leonardo have initiated a project:

Enhancing Public Understanding of Bioengineering Research and Applications

This poster serves as an initial report of that preliminary project.

Presented at Third Biomedical Engineering Education Summit Meeting
St. Charles, IL June 16, 17, 2008

Utah Science Center at The Leonardo

Fellows and Interns via
NASA Space Grant Universities Funds
May 6, 2008

Univ. of Utah Dept of Geography--GIS Program:

Justine Jedlicka: Vegetation, Biomes, Climate Change
Joe LaFollette: Water, Dams, Climate Change
Christy Heaton: Mosquitos, Disease, Climate Change
Phoebe McNeally: Faculty Advisor

Joe.andrade@utah.edu

Joe.andrade@utah.edu

Tropical Mosquito Related Diseases and the Effects of Global Warming

By Christy Heaton

Questions

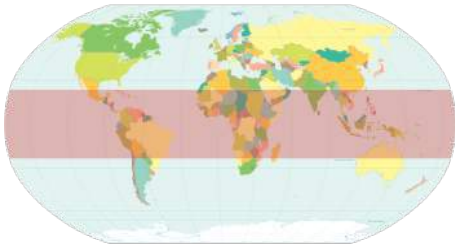
- What diseases are carried by mosquitoes?
- Where do these diseases occur?
- What is the ideal climate for these disease carrying mosquitoes?
- Will future climate change affect the areas in which these mosquitoes thrive?

What diseases are carried by mosquitoes?

- Malaria
- Yellow Fever
- Dengue Fever
- Rift Valley Fever
- Arboviral Encephalitis (includes West Nile Virus among others)

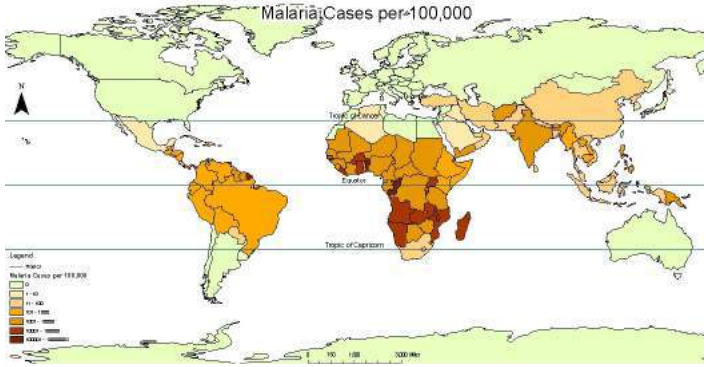
Where do these diseases occur?

- Apart from some types of Arboviral Encephalitis, these diseases occur predominantly in the tropics

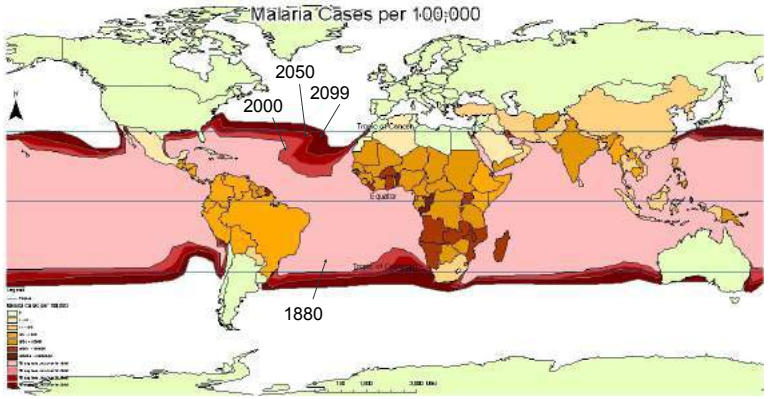


Case study: Malaria

- You can see that there are more cases of Malaria between the tropics of Cancer and Capricorn than anywhere else on Earth

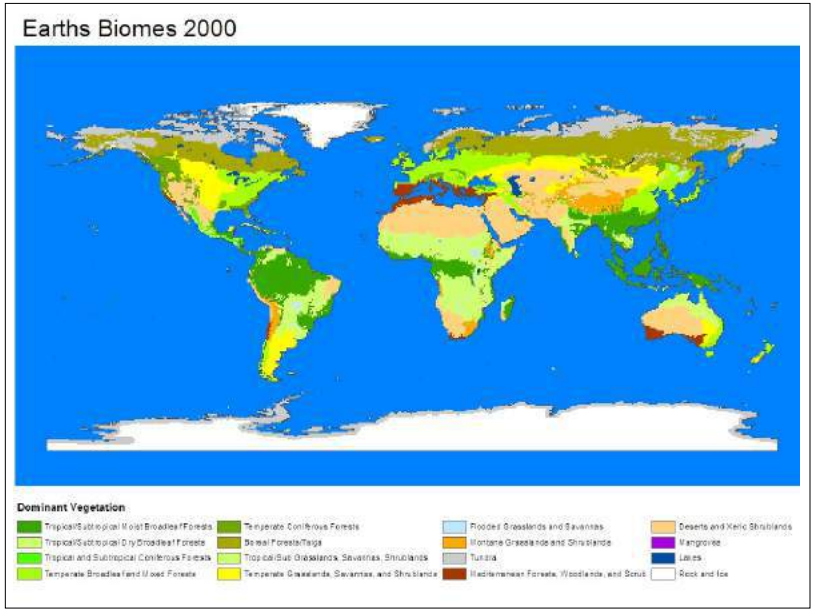


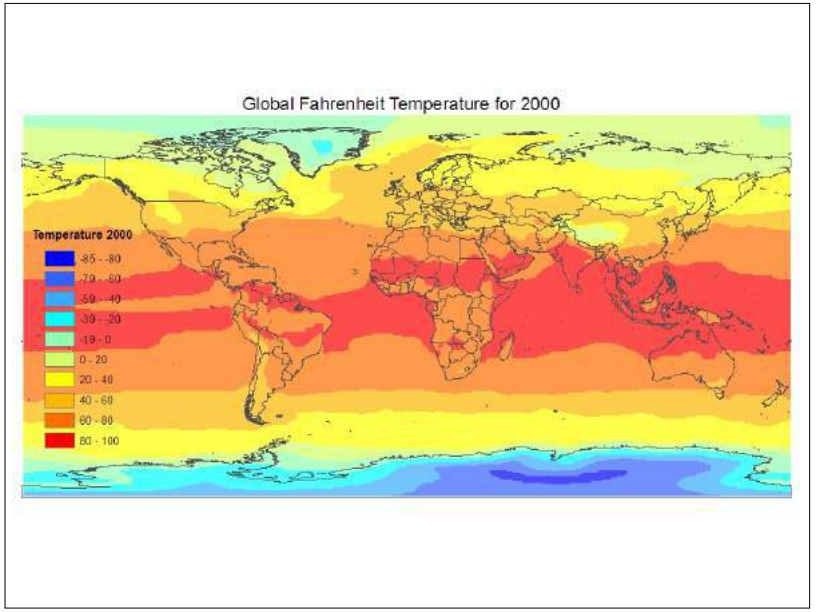
Will future climate change affect the areas in which these mosquitoes thrive?

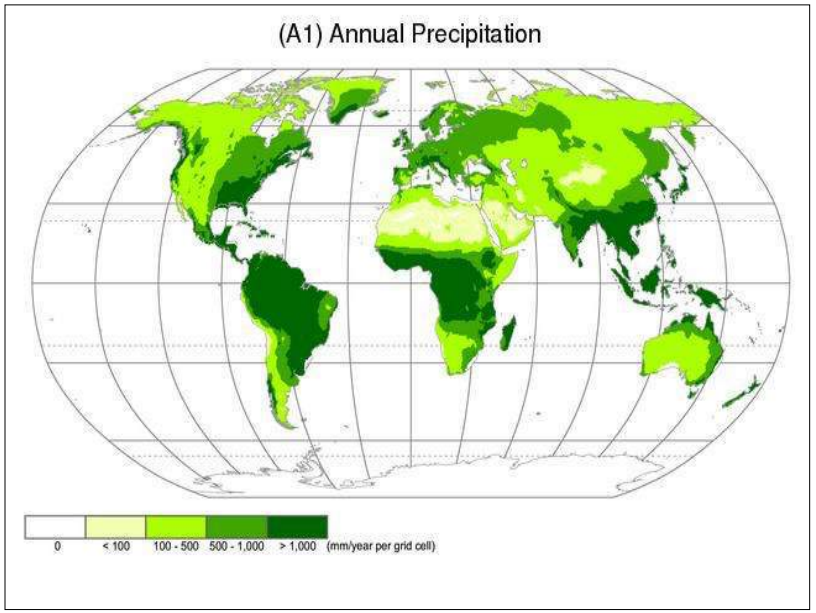


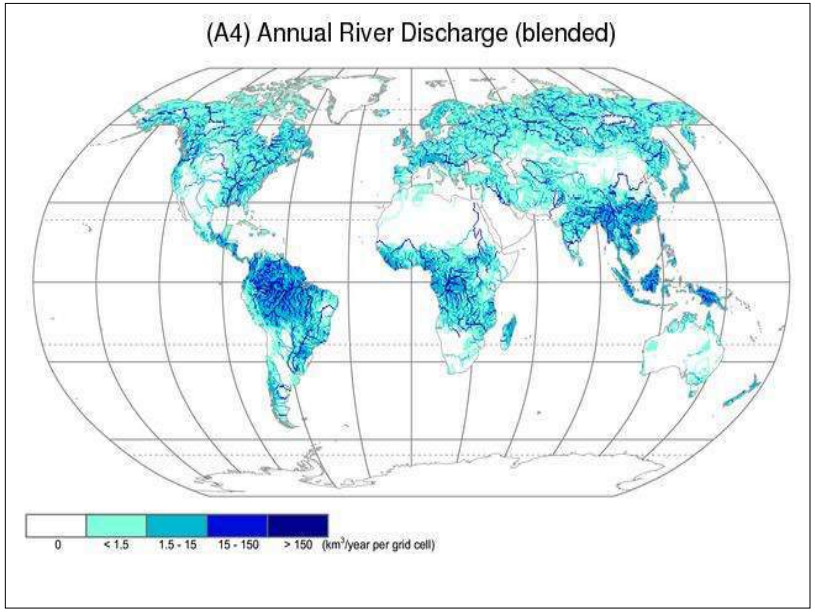
Conclusions

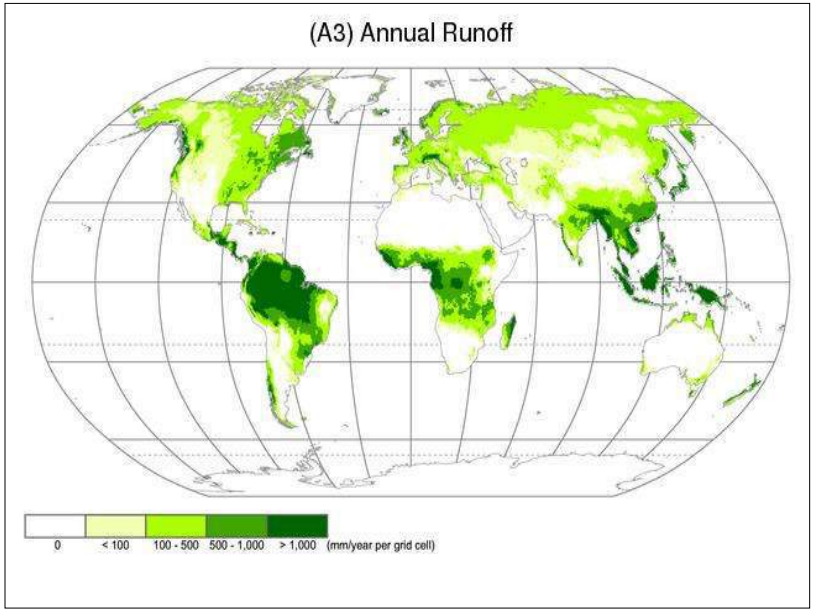
- Efforts should be made to reduce the warming trend in order to prevent the spread of disease and other potential effects
- Malaria eradication efforts have proved fruitless before, but if new methods are discovered, the spread of disease could be dissuaded despite climbing temperatures

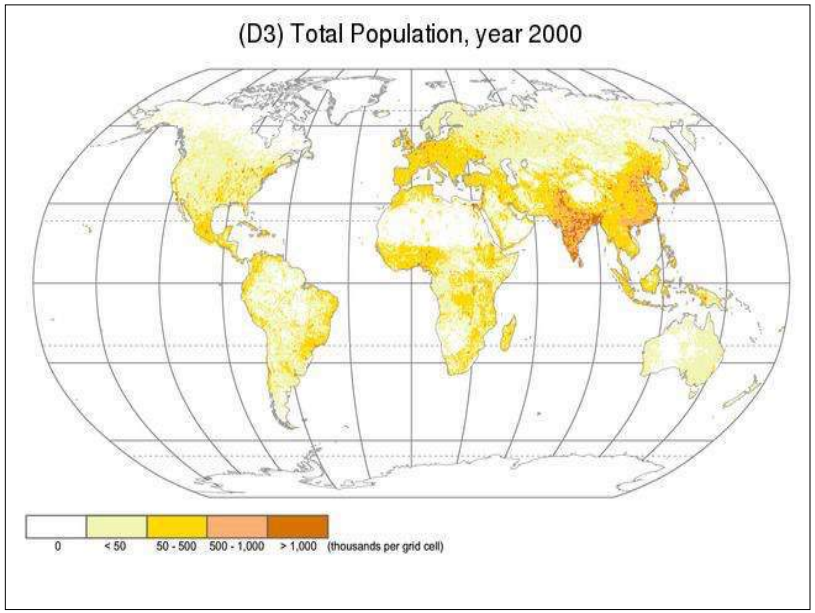

Earths Biomes 2000
Dominant Vegetation
Tropical/Subtropical Moist Broadleaf Forests
Tropical/Subtropical Dry Broadleaf Forests
Tropical and Subtropical Coniferous Forests
Temperate Broadleaf and Mixed Forests
Temperate Coniferous Forests
Boreal Forests/Taiga
Tropical/Sub Grasslands, Savannas, Shrublands
Temperate Grasslands, Savannas, and Shrublands
Flooded Grasslands and Savannas
Montane Grasslands and Shrublands
Tundra
Mediterranean Forests, Woodlands, and Scrub
Deserts and Xeric Shrublands
Mangroves
Lakes
Rock and Ice


Global Fahrenheit Temperature for 2000
Temperature 2000
-85 - -80
-79 - -60
-59 - -40
-39 - -20
-19 - 0
0 - 20
20 - 40
40 - 60
60 - 80
80 - 100


(A1) Annual Precipitation
0
< 100
100 - 500
500 - 1,000
> 1,000
(mm/year per grid cell)







THE ENERGY OF THE WORLD

An Examination of National & International Commercial Energy Production & Consumption Levels

Rosemary Fasselin

University of Utah

Department of Geography

April, 2007

Methodology

(A Cartogram of Sorts)

Weeks One Through Seven:

- Research
- Collect Data
- Make Contacts
- Look for Shapefiles
- Send E-mails
- Make Phone Calls

Decide to Use the Data that is Available (Change the Focus of the Project)

Weeks Eight & Nine:

Finish Collection of World Energy Data (Create Tables, et cetera)

Week Ten:

Edit Tables & Data.

Re-enter recently Updated Data

Weeks Eleven & Twelve:

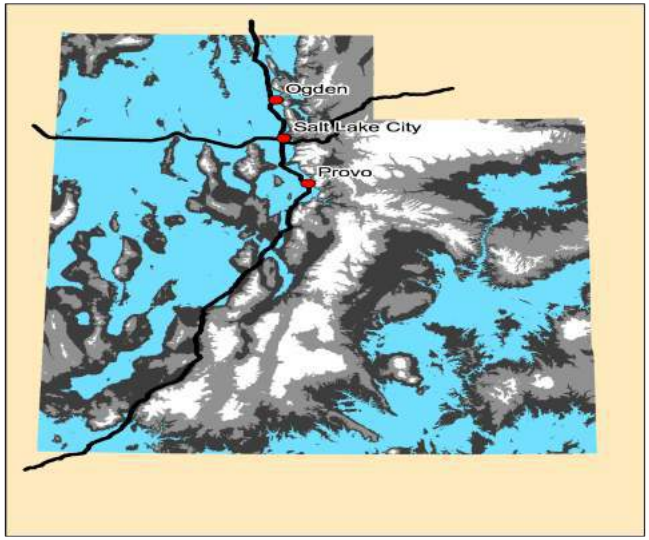
- Map Results, Write Reports & Presentation
- Join & Edit Shapefile Attribute Tables
- Double Check Accuracy

Utah's Winter Inversion

By Eric Barrow
Intern Leonardo Project

Purpose

Explain Salt Lake City's winter inversions and use GIS to show the accumulation of Pollutants during these events



Final Project
GIS 5140

Spatial Distribution of Mosquito Viruses

Michael Potter

Project Objectives

- Are incidents of West Nile virus related to locations near wetlands?
  - Other factors involved
- If examined at the county level, will the same results hold true at the state level?
  - Utah
  - Idaho
  - Nebraska
- West Nile virus distribution on a national level
- Malaria cases on a world wide level

Earth, Utah, The Leonardo -- Better Pictures, Better Stories

Joe Andrade*, Laura Shearer, Sose Matuauto, Jeremy Smith, and Jake Hanson
University of Utah, Salt Lake City, UT 84112 and
*Department of Bioengineering and The Leonardo - Science, Salt Lake City, UT 84111





The Leonardo

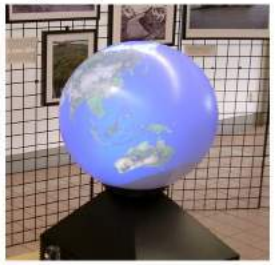
A functioning democracy requires a literate, aware, educated, involved, and responsible electorate. Because the general public is very interested in geongraphy, mapping, and - more recently - in the stability and viability of Planet Earth, these subjects provide an avenue for enhanced and expanded activities related to scientific and technical literacy.

Science Centers provide opportunities for the general public to experience, participate, and learn a wide range of science and engineering fields.

The Leonardo -- opening in 2010 or early 2011 in Salt Lake City - is a major center for science, art, and culture—taking interactivity and personal involvement to an entirely new level.

The Leonardo's Center for the Big Picture (CBG) is focused on helping visitors develop global and systems-based perspectives of complex and multi-variate problems and issues. CBG will include the Science on a Sphere planetary visualization technology, now being widely applied in science centers and museums, as well as flat and touch screen components permitting effective use of GIS, GoogleEarth, and related zooming/layering approaches. We are also employing Leonardo's ideas of 'New Ways of Seeing' - saper vedere - as well as enhanced ways of seeing, via caricatures, such as available via www.worldmapper.org


Science on a Sphere at Clark Planetarium

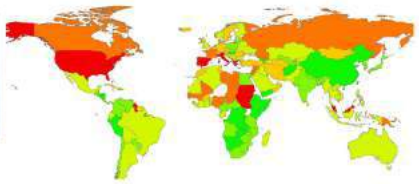

Magic Planet at The Leonardo

Stories and People:

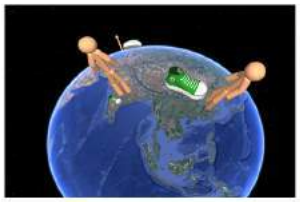
SlavePower: 1700s to Now is Laura Shearer's map-empowered story, tracing trade routes for energy, people, and work and relating Colonialism to Globalization in an energy-intensive context. She uses a SlavePower 'footprint' to help make the point.

Babies, People, Cultures and Energy is Sose Matuauto's story, connecting birth rates, population, and per capita energy use in the context of energy as related to cultures, religions, and civilizations. She is developing baby/people 'footprints' to see the impact and the problem

Treading Water: What's YOUR 'Shoe' Size? is Jeremy Smith's story on waters, rivers, and usage, as related to climate change, river systems, and population, as well as drought and agriculture.



Affluence, Footprints, Climate Change, and Policy is Jacob Hansen's story - tying material consumption in the American economy to eco- and carbon-footprints and climate change- and suggesting personal and public policy approaches.



Bigger and Better 'Pictures'

We are developing a variety and range of Big Picture interactive stories and presentations for The Leonardo and its workshop-based traveling and community events. ENERGY - the BIG Picture is the first of these. We need volunteers to help with these ambitious plans for helping to develop public interest, awareness, motivation, and involvement. Contact us at:
Joe.andrade@utah.edu 801-706-6747

The University's research and education mission extends to its general public and community. Most Universities have 'outreach' and related programs with which to involve, inform, and educate the greater community. Service learning and related community involvement activities are generally fostered and encouraged. University of Utah programs involved with The Leonardo include:

Bioengineering	Biology	Chemistry	Geography
Meteorology	Pharmacy	Physics	Psychology
Electrical Engrg	Computer Sci		

References and More Information:

www.worldmapper.org

www.globalimagination.org

www.utahsciencecenter.org

www.theleonardo.org

Support The student interns have been supported by a grant from the Rocky Mountain NASA Space Grant Consortium

Presented at UGIC 2009, Zermat, Midway, Utah

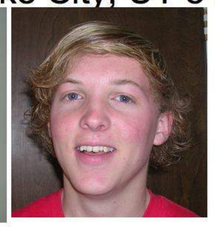
http://utahsciencecenter.org/utahsci/documents/UGIC_poster.pdf

Earth, Utah, The Leonardo -- Maps, Pictures, Stories

Joe Andrade*, Jake Hanson, Lauren Wood, Austin Coates, Blake Huff,
Patrick Engberson, and Ambrea Kuhn University of Utah, Salt Lake City, UT 84112 and
*Department of Bioengineering and The Leonardo, Salt Lake City, UT 84110






The Leonardo

A functioning democracy requires a literate, aware, educated, involved, and responsible electorate. Because the general public is very interested in geography, mapping, and - more recently - in the stability and viability of Planet Earth, these subjects provide an avenue for enhanced and expanded activities related to scientific and technical literacy.

Science Centers provide opportunities for the general public to experience, participate, and learn a wide range of science and engineering fields.

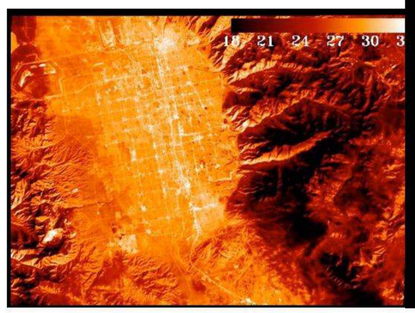
The Leonardo -- opening in 2011 in Salt Lake City - is a major center for science, art, and culture—taking interactivity and personal involvement to an entirely new level.

The Leonardo's programs will help visitors develop global and systems-based perspectives of complex and multi-variate problems and issues, making effective use of dynamic planetary visualization, GIS, GoogleEarth, and related zooming/layering approaches. The Leonardo is also employing Leonardo's ideas of 'New Ways of Seeing' - saper vedere - as well as enhanced ways of seeing, via caricatures, such as available via www.worldmapper.org

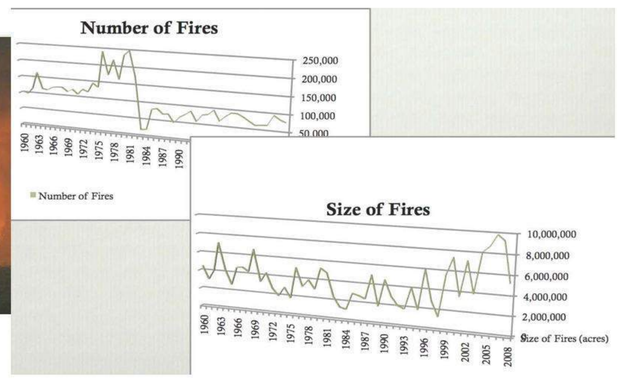

Science on a Sphere at Clark Planetarium Magic Planet at a The Leo event

Stories and Projects

Urban Heat Islands: Why Does My Ice Cream Melt Faster in The City? is Austin Coates' project. He considered the factors contributing to urban heat and means to minimize and alleviate it.

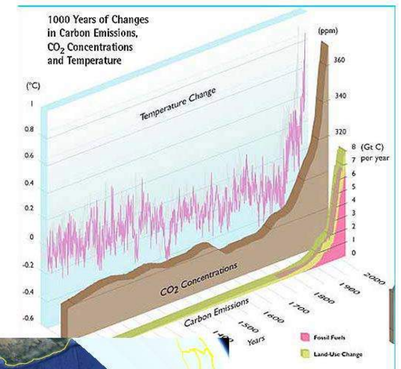


Vegetation Management: Conservation or Preservation is Blake Huff's project. Blake covered the factors influencing vegetation coverage and types, in Utah and on the entire Planet. He also noted changes due to humans and climate change, as well as forest fire issues (Blake is a forest firefighter).

Joe Time Travel, Lauren Wood's project looks at carbon footprints through the Holocene, from nomads to modern man, and looks at resource disparities between advanced and third world nations, using Haiti as an example. She uses Google Earth, cartoons, and a historical approach. See pictures at top left.

Ambrea Kuhn and Patrick Engberson have produced *short videos* related to STEM (Science, Technology, Engineering, Math) careers and on the principles of energy transformation and energy 'behavior' - dealing with responsible energy practices.



Better 'Pictures' and Stories

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