Visualizing Multi-Analytical Clinical Diagnostic Data via Simple Patterns

Journal:	*AMIA 2008 Annual Symposium*
Manuscript ID:	draft
Manuscript Type:	Student Paper
Date Submitted by the Author:	n/a
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Visualizing Multi-Analytical Clinical Diagnostic Data via Simple Patterns

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Abstract

Multi-analytical clinical data can be displayed via simple patterns to ease interpretation and enable fast diagnostic decision-making. We developed and employed a software program "MACROPatterns" (Multi-Analytical Chemistry-Recognizer of Optical Patterns) for this purpose. MACROPatterns is a multi-dimensional visualization program that enables simultaneous interpretation of measurements along with the recognition of correlated or uncorrelated patterns. Employing visualization concepts and approaches in MACROPatterns required knowledge in various fields, including visual cognition and recognition, art, scientific visualization, and software design. MACROPatterns provides easy navigation through different pathologic panels and various patterns of each panel. This could be very useful especially in clinical education and training. MACROPatterns can be utilized in different analytical fields that require interpretation of multiple measurements along with the recognition of correlated or uncorrelated patterns. Multi-analytical clinical chemistry data visualization via simple iconic displays is demonstrated in the diagnosis of galactosemia and hyperlipoproteinemia.

Introduction

High-dimensional data visualization presents a large number of dimensions or parameters of the data on a display surface (soft or hardcopy). High dimensional data visualization projects n dimensional data onto a 2D physical medium.[1-6] Multi-analytical clinical data can be displayed via simple patterns to ease interpretation and enable fast diagnostic decision-making.[7-12] Wolfgang Vogt is one of the pioneers in clinical data display. Diagnosing hyperthyroid disease is a good example of his work.[13-15] In the example of diagnosing hyperthyroidism, after the tentative diagnosis of a hyperthyroid situation has been made, free thyroxine (FT_4) and free triiodothronine (FT_3) are investigated and one (or both) of these clinical chemical parameters is supposed to be elevated. Hence a diagnostic model can be formulated:

- Grave's Disease $\Leftrightarrow$ {High FT_4 & High FT_3}; where & refers to a joint state
- Thyroiditis $\Leftrightarrow$ {High FT_4 & High FT_3}
- T_4 Thyrotoxicosis $\Leftrightarrow$ {High FT_4}
- T_3 Thyrotoxicosis $\Leftrightarrow$ {High FT_3}
- Increased Thyroxine-Binding Globulin (TBG) $\Leftrightarrow$ {High FT_4 & High FT_3}

Clearly, a definite diagnosis is impossible because the attributes in the premise are not sufficient. Therefore, further attributes like FT_3 fraction-uptake by analytical method, thyroid-stimulating hormone (TSH), and FT_4 index (FT_4I) have to be added and the process has to be repeated for further clarification. Junctions of such attributes may be called a pattern. Of course, such patterns can also be put into premises. The maximum information content can be achieved if every clinical chemical parameter is determined. This corresponds to an exhaustive procedure with high redundancy and cost. Further, it is impossible simultaneously to detect interrelationships between more than 3D to 5D data. The information from a single value of a parameter can be clearly realized, but the information due to a combination of different quantitative values cannot. Therefore, it is important first to find procedures that help the physician to choose suitable clinical chemical parameters for the solution of a certain diagnostic problem, and second to transform information contained in the single values into general information on one visual display.[13-15]

Stimulated by Vogt's work, we hoped to find appropriate means to represent data generated from a clinical chemistry chip via simple, yet powerful visual patterns. Thus, we developed a software program capable of mathematically and graphically transforming the clinical chemistry chip's data into simple, recognizable visual diagnostic patterns. We called this program MACROPatterns (Multi-Analytical Chemistry-Recognizer of Optical Patterns).

MACROPatterns

MACROPatterns is a multi-dimensional visualization program that enables simultaneous interpretation of measurements along with the recognition of correlated or uncorrelated patterns. Employing visualization concepts and approaches in MACROPatterns required knowledge in various fields, including visual cognition and recognition, art,

scientific visualization, and software design. Visualization concepts and approaches include:

1) Visual perception; human visual perception performs best at one-dimensional space, and the larger the dimensionality of space is, the weaker human visual perception becomes,

2) Visual recognition; displaying and adding attributes to useful data, and

3) MACROPatterns functionality; projecting useful data onto a two-dimensional physical medium, clustering data into simple visual patterns, adding attributes (color, brightness, transparency, or shape distortion) to patterns, and displaying multiple patterns on one screen to ease comparative interpretation.[7]

MACROPatterns provides easy navigation through different pathologic panels and various patterns of each panel. This could be very useful especially in clinical education and training. It assigns the term "Panel" to all analytes related to a clinical condition, and assigns the term "Patterns" to comparative displays (or maps) of the panel's measurement results "Pathological (or the name of the corresponding sub-disorder)" versus (vs. or v.) normal values "Reference" and a cluster of sub-disorder "Diagnostic": Reference vs. Diagnostic (R v. D); Diagnostic vs. Pathological (D v. P); Reference vs. Pathological (R v. P); and Reference vs. Diagnostic vs. Pathological (All). Using MACROPatterns to display multi-analytical clinical data is demonstrated in two cases: galactosemia and hyperlipoproteinemia.

MACROPatterns Demonstrated

Galactosemia: Galactosemia is an inherited disease in which galactose (Gal) and the derived toxic products galactose-1-phosphate (Gal-1-P), galactitol, and galactonate accumulate in the blood due to enzymatic deficiency. The severe form (classical galactosemia) is a life threatening disease resulting from lack of Gal-1-P uridyltransferase (GalT) caused by genetic mutation. Classical galactosemia is suspected when the initial screening shows a galactose value higher than 20 mg/dl and/or GalT absence. Galactosemia may also be caused by a deficiency of UDP-Galactose-4'-epimerase (GalE) associated with increased levels of galactose and Gal-1-P, or a deficiency of galactokinase (GalK) associated with increased levels of galactose, Gal-1-P, galactitol, and galactonate, see Table 1.[11-12, 16-21]

MACROPatterns can be used to display patterns of a galactosemia panel consisting of galactose, GalK, GalT, GalE, and Gal-1-P along with a map of all the patterns of classical galactosemia (see Figures 1 and 2).

Table 1. Galactosemia Diagnosing Panel[7]

	Gal	GalK	GalT	GalE	Gal-1-P	Galactitol	Galactonate
Galaktokinase-deficient galactosemia	+ + +	- - -	Normal	Normal	+ +	+ + +	+ + +
G-1-P uridyltransferase-deficient galactosemia	+ +	Normal	- - -	Normal	+ + +	+ + +	+ + +
UDP-galactose-4'-epimerase-defecient galactosemia	+ +	Normal	Normal	- - -	+ +		

Hyperlipoproteinemia: Hyperlipoproteinemia is abnormally high levels of lipids (cholesterol, triglycerides, or both) carried by lipoproteins in blood; low density lipoprotein (LDL) cholesterol, very low density lipoprotein (VLDL) cholesterol, and chylomicrons. However, a high level of the high density lipoprotein (HDL) cholesterol "the good cholesterol" is beneficial and is not considered a disorder. Levels of lipoproteins increase slightly as people age. Also, they are normally slightly higher in men than in women, but increase in women after menopause. The increase in levels of lipoproteins occurring along with aging can result in hyperlipoproteinemia and increase the risk of atherosclerosis.[16, 22]

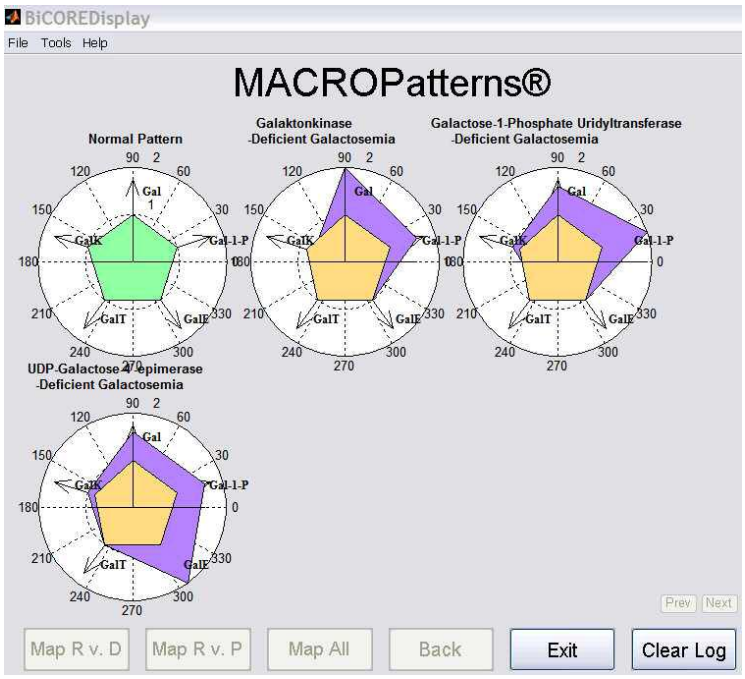

Figure 1. Four iconic displays for the patterns associated with galactosemia: The upper left display is the reference pattern, the other three displays show diagnostic patterns imposed on top of the pathological patterns of patients.[7]

Figure 2. A comparative display of patterns related to galactokinase-deficient galactosemia: The small polygon refers to the typical diagnostic pattern of galactokinase-deficient galactosemia. The pentagon refers to the reference pattern of the extended galactosemia panel. The big polygon is the patient's pattern.[7]

Columns of Table 2 represent the hyperlipoproteinemia panel, whereas the rows represent the diagnostic patterns. This case is uniquely processed in MACROPatterns; unlike the other analytes of the hyperlipoproteinemia panel, chylomicrons are qualitatively analyzed in urine samples. Typically, chylomicrons are reported either as negative (clear urine) or positive (creamy urine). Thus, MACROPatterns assigns chylomicrons an axis with 0 or 1 values. Also a color dimming attribute is added to the diagnostic and patient patterns to reflect the positive (or creamy) values of chylomicrons. Therefore, when chylomicrons exist (positive result) the corresponding diagnostic pattern would appear dimmer towards the 1 value on the chylomicrons axis (see Figures 3 and 4).

Table 2. Hyperlipoproteinemia diagnosing panel[7]

	Chylomicrons	LDL	VLDL	Cholesterol	Triglycerides
Hyperchylomicronemia	+ +	Normal	Normal	Normal or +	+ + +
Hyperbetalipoproteinemia	Normal	+ + +	Normal	+ + +	Normal
Combined Hyperlipoproteinemia	Normal	+ + +	+	+ + +	+
Hyperprebetalipoproteinemia	Normal	Normal	+ + +	Normal or +	+ + +
Mixed Hyperlipoproteinemia	+ +	Normal	+ + +	+ + +	+ +

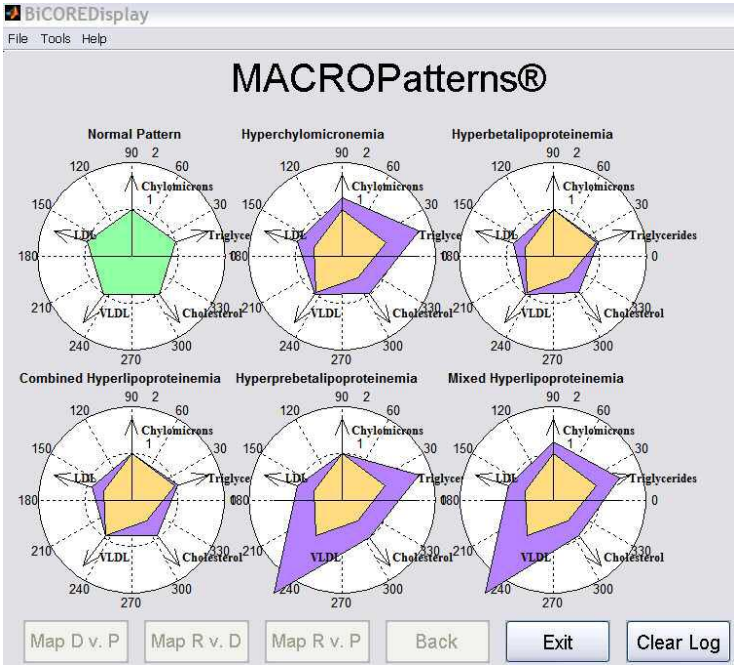

Figure 3. Six iconic displays for the patterns associated with the hyperlipoproteinemia: The upper left display is the reference pattern, the other five displays show diagnostic patterns imposed on top of patients' pathological patterns.[7]

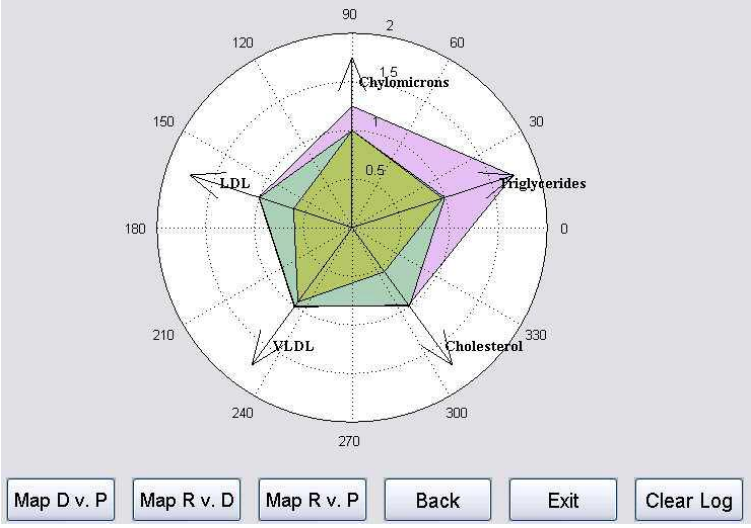

Figure 4. A comparative display of patterns related to hyperchylomicronemia: The small polygon refers to the typical diagnostic pattern of hyperchylomicronemia. The pentagon refers to the reference pattern of the extended hyperlipoproteinemia panel. The big polygon is the patient's pattern.[7]

The existing version of MACROPatterns and its documentation are available on AL-sheikh's webpage: (http://informatics.bmi.utah.edu/wiki/index.php/User:YTAL). The program is not being improved or supported.

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Submission Confirmation

Thank you for submitting your manuscript to *AMIA 2008 Annual Symposium*.

Manuscript ID:	AMIA-0824-A2008
Title:	Visualizing Multi-Analytical Clinical Diagnostic Data via Simple Patterns
Authors:	AL-sheikh, Youssef Andrade, Joseph
Date Submitted:	14-Mar-2008

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