Visualizing Multi-Analytical Clinical Chemistry Data via Simple Patterns

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Abstract

Multi-analytical clinical chemistry 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 multidimensional 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 and 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 laboratory 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.

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.[7-14] Wolfgang Vogt is one of the pioneers in clinical data display. Diagnosing hyperthyroid disease is a good example of his work.[15-17] In the example of diagnosing hyperthyroidism, after the tentative diagnosis of a hyperthyroid situation has been made, free thyroxine (FT4) and free triiodothronine (FT3) 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; {High FT4 & High FT3}; where "&" refers to a joint state.
- Hashimoto's Disease; {High FT4 & High FT3}.
- T4 thyrotoxicosis; {High FT4}.
- T3 thyrotoxicosis; {High FT3}.
- Increased thyroxine-binding globulin (TBG); {High FT4 & High FT3}.

Clearly, a definite diagnosis is impossible because the attributes in the premise are not sufficient. Therefore, further attributes like FT3 fraction-uptake by analytical method, thyroid-stimulating hormone (TSH), and FT4 index (FT4I) 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.[15-17]

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 and scientific visualization, and software design.

Table 1_Galactosemia Diagnosing Panel[7-9]	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	- - -	+ +		

Concepts: MACROPatterns visualization concepts and approaches include:

1) Visual perception: human visual perception performs best at 1-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 2-dimensional physical medium, clustering data into simple visual patterns, adding attributes (color, brightness, transparency, or shape distortion) to patterns, and displaying multiple patterns on 1 screen to ease comparative interpretation.[7-9]

Environment: 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":
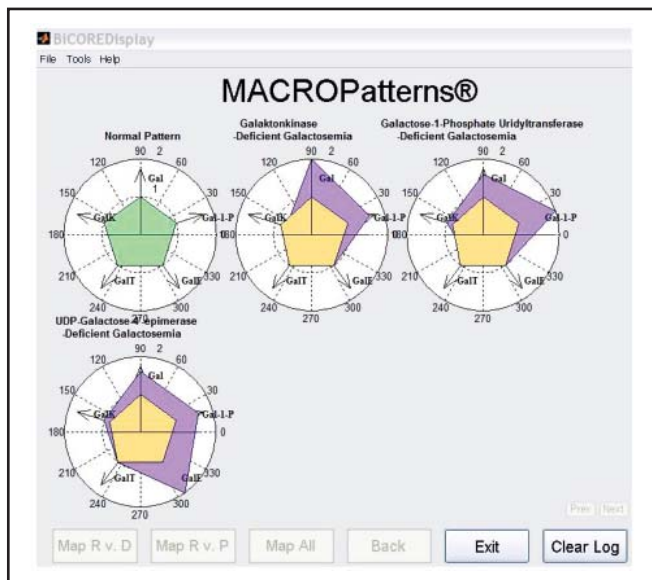
- Reference vs. Diagnostic (R v. D);
- Diagnostic vs. Pathological (D v. P);
- Reference vs. Pathological (R v. P); and
- Reference vs. Diagnostic vs. Pathological (All).

Using MACROPatterns to display multi-analytical clinical data is demonstrated in 2 cases: galactosemia and hyperlipoproteinemia.

Clinical Examples

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 (**Table 1**).[13-14,18-23] 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 (**Figures 1** and **2**).

Figure 1_ Four iconic displays for the patterns associated with galactosemia. The upper left display is the reference pattern; the other 3 displays show diagnostic patterns imposed on top of the pathological patterns of patients.[7-9]

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.[7-9]

Table 2_Hyperlipoproteinemia Diagnosing Panel[7-9]

	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	+ + +	+ + +	+ +

LDL, low-density lipoprotein; VLDL, very-low-density lipoprotein

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.[18,24]

Columns in **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 (**Figures 3** and **4**).

If further developed to visualize measurements of other clinical measurements, MACROPatterns may be a useful software program aimed towards enabling differential diagnoses of complex diseases and in training clinicians. The reader is referred to a Web site (www.DiabetesInfoPortal.org) for further details on the design and development of MACROPatterns, and for downloading version 1.0 of the software program and the associated user manual. LM

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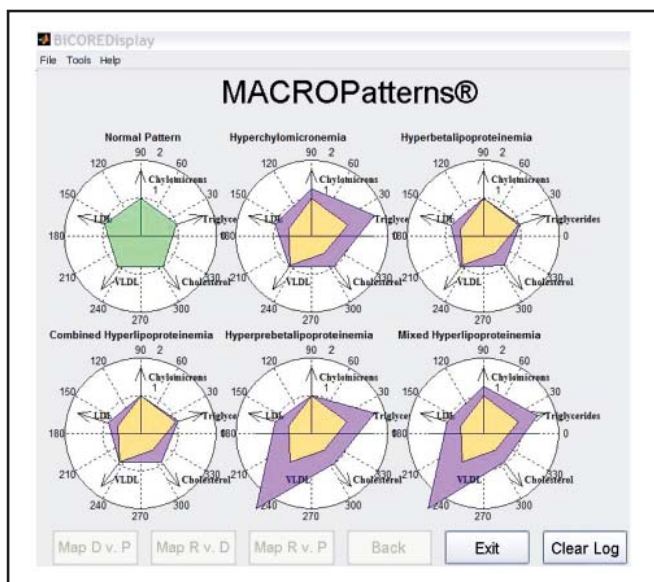
Figure 3_ Six iconic displays for the patterns associated with the hyperlipoproteinemia. The upper left display is the reference pattern; the other 5 displays show diagnostic patterns imposed on top of patients' pathological patterns.[7-9]
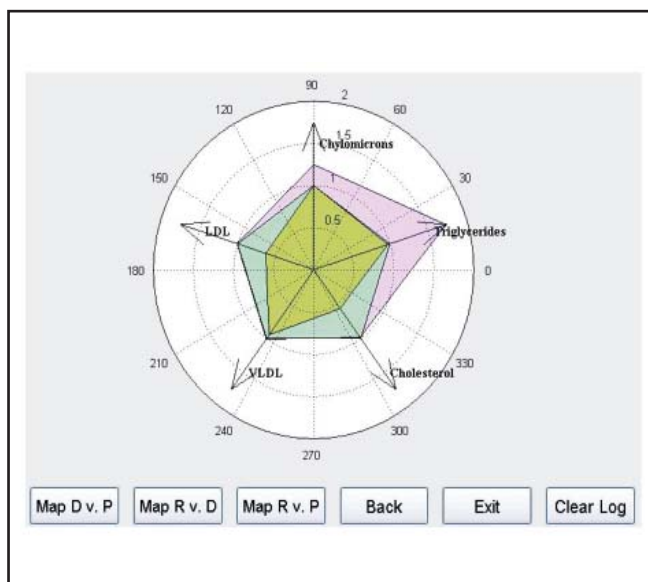
Figure 4_A comparative display of patterns related to hyperchylomicronemia. The small polygon refers to the typical diagnostic pattern of hyperchylomicronemia. The pentagon refers to the reference pattern of the extended hyperlipoproteinemia panel. The big polygon is the patient's pattern.[7-9]

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