

## **METABOLOMICS**

**Where do we come from? Who are we? Where are we going**

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(with apologies to Paul Gauguin)

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### **ABSTRACT**

The evolving “Omic-Metabolomic” hypothesis of disease is that it is a failure of feedback control among the genome, transcriptome, proteome and metabolome-what we call disease is symptoms that occur as a result of the control failure-the pattern and relationships of the small molecules regulating signaling and reflecting processes (the Metabolome) will define this failure of control.

Where do we come from? We will discuss the characteristics and current capabilities of the Liquid Chromatography Electrochemical Array (LCEC) and combined LCEC with Mass Spectrometry platforms used by our group, covering: the nature of the data; problems of identification of the statistically significant structural unknowns from profiles of ca.1500 compounds at pg/ml levels; techniques of data reduction, validation and analysis. Use examples will be taken from studies of classification and sub classification of neurodegenerative diseases, prediction of therapeutic outcome in depression, comparison of animal disease models and human profiles and evaluation of individual specificity of the Metabolome.

Who are we? The Metabolome is complex and not fully defined by any one technology. We are a small piece of the “Metabolomics Network” a consortium of multi center multi technology capabilities. We will discuss: some of the programs; the various platforms available; the promise and problems of integrating data from multiple platforms.

Where are we going? What we know from, and what we’ve had to do these studies is dwarfed by what we don’t know and think we need as a result of doing them.

Some topics and notions in technologies: A universal device/protocol for sample acquisition in large scale studies; More sensitive sensors and faster protocols to reopen the hypothesis for sporadic production of endogenous neurotoxins; sample preparation devices to investigate metabolite distribution.

Some topics and notions in concepts: Are the words Disorder and Target semantic traps for thinking about the nature of disease and the development of therapeutics; is there an unexplored class of biomarkers reflecting metabolomic/proteomic/genomic interactions that will provide insight into epigenetic factors in disease; does your genome define your gut microbiome/gut metabolome and what are the implications for diagnostics and therapy.

### **Informal Biosketch**

My interest is developing/using technology to find and control disease risk factors in the general population.

I trained at MIT from 1960-1967 and spent the last 55 years trying to get educated. In 1968 I went to the Univ. of Michigan studying the transport and ubiquity of toxic metals in the environment and people-winding up at the bottom of the Faculty Food Chain as an Asst. Prof. in the School of Public Health.

Tired of studying problems, in 1970 I co-founded ESA Inc. to do something about childhood lead poisoning. If your kid gets their finger stuck before entering Kindergarten it’s partly my fault.

As technical director at ESA (once described as the oldest start up in Massachusetts) from 1970-2005 we developed devices for childhood lead insult and iron deficiency, detectors, separations research, and various novel diagnostics. Along the way I got educated on the workings of the US congress, got a couple of IR100 awards and was stuck onto some 100 papers and 100 US and Foreign patents-most of the latter as a result of laboratory mistakes.

In 1989 I started using electrochemical array technology in the field of “measuring lots of stuff and trying to figure out what it means”. This was called Metabolomics around 2000-mostly because you can get funded for “Omics”. In 2005 after ESA was sold I went to the non-profit Bedford Research Corp. at the Bedford VA to develop and direct systems biochemistry programs studying Metabolomics for disease diagnosis and therapeutic development.

Tired again of just studying problems I basically regressed four decades and in 2013 co-founded Counterpoint Health Solutions to systematically identify chronic disease risk factors and figure out ways to control them-which if nothing else has delayed any possible retirement.