19th Altenberg Workshop in Theoretical Biology 2008

Measuring Biology
Quantitative Methods: Past and Future

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organized by Fred L. Bookstein and Katrin Schaefer

Konrad Lorenz Institute
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The topic

Just fifty years ago the historian of science Harry Woolf edited the slim volume *Quantification: A History of the Meaning of Measurement in the Natural and Social Sciences* in which Thomas Kuhn first sketched his approach to the centrality of quantitative anomalies in the progress of science. Just a few years later there appeared Wigner's wonderful phrase about the "unreasonable effectiveness of mathematics in the natural sciences." Here in 2008, our understanding of science as a social system has been utterly transformed, and yet the role of numbers themselves has not come under much sustained scrutiny.

So this KLI workshop comes at a propitious time in a propitious locale. If science studies are relatively silent on quantification, the rest of us can speak as practitioner-scholars. At the same time, the explosion of biological information resources, more sudden than the corresponding transition in any other field, has made the search for a re-foundation of quantitative methods most compelling just where it overlaps with our own cognitive limitations. Biological information resources are expanding at an enormous rate, but likewise the data density of the scientist's tools of exposition. The quantitative load of our presentations thus grows at least as fast as our data resources themselves. All this is overdue for serious interdisciplinary study; hence this workshop.

We are organized in five sessions. The central three are an attempt at sorting the current universe of biologically salient measurements into three broad streams: the new raw quantifications from (gen)omics and (dyn)amics, evolution and development, and environment and behavior. Preceding these is an opening session on philosophical and historical foundations; just prior to the closing Discussion is a pair of talks on consequences for method and implications for the sciences in their broadest public context.

Program

PHILOSOPHICAL & HISTORICAL FOUNDATIONS

Rodrigo J. De Marco A suitable foundation for theories dealing with biological systems
György Darvas The unreasonable effectiveness of symmetry in the sciences

THE NEW BIOLOGY OF QUANTIFICATION

Richard Gordon Building quantitative understanding of an embryo as it builds itself
Clive E. Bowman Megavariate genetics: What you find is what you go looking for
Harald Martens Bio-chemometrics: Finding dynamics and harmonics in the cacophony of data from molecular biology

TWO EXPLANATIONS AT ONCE: EVOLUTION AND DEVELOPMENT

Benedikt Hallgrimsson Measurement, morphology and mechanism: Why developmental biology needs morphometrics
Charles Oxnard Biology certainly needs morphometrics: Does morphometrics need biology?
Philipp Mitteroecker The concept of morphospaces in evolutionary and developmental biology

TWO EXPLANATIONS AT ONCE: ENVIRONMENT AND BEHAVIOR

Katrin Schaefer Psychomorphospace: From biology to perception and back
Rafael Núñez Numbers and quantification: Where do they come from?
Magni Martens Human senses in action: Multivariate measurements of quality

CONSEQUENCES FOR METHODS AND REFLECTIONS

Deirdre McCloskey The unreasonable ineffectiveness of Fisherian statistics in biology and the social sciences
Fred L. Bookstein Measurement, explanation, and biology: Lessons from a long century

Abstracts

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Measurement, explanation, and biology: Lessons from a long century

Statistics, characterized at its most abstract level, is the logic of uncertainty as applied to quantitative measurements. It is far from obvious that, beyond the timeless invocations by animal breeders and the like, this style of reasoning would ever be of any use in biology. The methodological possibility of an effective biometrics was not seriously raised until well into the twentieth century, long after formal statistical reasoning had been firmly established as one foundation of the physical sciences and, in another costume, as one of the foundations of statecraft. Biometric statistics has been the last branch of academic statistics to emerge, and morphometrics, the field with which I am most closely identified, is the most recent innovation of biometrics, elementary even when I wrote the first book on the modern treatment of the subject in 1978.
Nevertheless, here in 2008, it must be conceded that statistical reasoning is a crucial ingredient in the logical foundation underpinning contemporary biological sciences. The apparently effective styles of statistical reasoning in biology and medicine contribute not only to morphometrics but also to clinical epidemiology, global systems analysis, and most of the new domains usually referred to semantically as "-omics". Paradoxically, in all these arenas, biostatistics gains power by explicitly ignoring or downplaying most of the features that we already know to be true about biological systems in their actual real-world context: path-dependence, irreversibility of historical change, and stabilization of initially random explorations of configuration spaces. The success of statistical methods, in other words, comes at the expense of all the theories that we simultaneously hold to be true about the biological materials to which they both pertain.
My talk, coming at the end of our workshop, will explore this fundamental antinomy in light of most of the contributions preceding it. Earlier discussions of this problem by the physicist Walter Elsasser and others have emphasized the way in which biophysical reductionism applies in biology but fails to govern. In this talk I will explore an alternative trope based on the way that statistics represents uncertainty across most of its domains of application, not only those in the natural sciences. Statistics proves a surpassingly effective tool, in other words, for the exploration of small, ahistorical effects on systems whose principal determinants are utterly lost in the antiquity of aeons. The power of these methods is founded rather in their lability as regards all the different languages in which biological systems can have their stability characterized: languages as disparate as Baupläne, enzymatic networks, or folding patterns of proteins.
Statistics seems to work in biology by swimming starkly against the tide of reductionism that otherwise drives change in the domains of speediest progress.
Why this should be the case—how biometrics and biostatistics can thrive independently of the sciences of biological structure, or even in conceptual opposition to them—is a question that can only gain salience here in the new century.

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Megavariate genetics: What you find is what you go looking for

The inherent subjectivity of measuring biology is posed using examples from high-dimensional genetic research. The human observer is integrally embedded in the ascertainment, referential basis, kernel choice, feature search and cognitive display for such quantitation. Reductionism is operational not intrinsic — individuality infers that the gestalt is supreme. Despite, the fact, that 'there is nothing but what you think there is' — Popper rules!

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The unreasonable effectiveness of symmetry in the sciences

- Philosophical approach: the question of primacy (mathematics vs. nature).
- Wigner on the relation of invariance (symmetry) and mathematics, as well as on the domain of their applicability in the sciences: wider or narrower?
- Wigner's position on the effectiveness of symmetry in the physical laws of nature. (Hamming's position.)
- Van Fraassen: Laws of nature or symmetry principles?
- The effectiveness of symmetry principles beyond physics.
- Symmetry principles and the quantification in the sciences.
- Emergence: quantifiable or purely qualitative phenomenon?
- A symmetrist's ontological approaches to the problems of evolution: evolution of matter (structural approach), symmetry breaking and evolution in living matter (morphological approach), protein synthesis (genetic evolution), the human brain (functional symmetry breaking).
- A symmetrist's epistemological approach: consequences of the dissymmetric and antisymmetric cerebral functions in human perception, learning and research.
- Feedback to obtaining knowledge about the objective world: human influences or pure mathematics? (Left- and right-hemisphere dominated approaches to a given problem: interpretations, e.g., wave or corpuscle, wave-mechanics or matrix-mechanics, continuous evolution or sequence of spontaneous mutations in the organic world, evolution or revolution in society.) Kant's a priori categories and antinomic pairs, M. Polányi's personal knowledge, or K. Popper's objective knowledge?
- Mathematical description of qualitative changes by means of group-theoretical methods, elaborated for symmetry studies.
- The contribution of symmetry principles to resolve the dichotomy whether qualitative or quantitative methods were more effective in the sciences.

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A suitable foundation for theories dealing with biological systems

I will argue that the philosophy appropriate for the physical sciences is unsuitable as a foundation for theories dealing with biological systems. This happens because biological systems are essentially complex, in that they involve amounts of components and nonlinear interactions that are simply beyond measure. Indeed, the task of optimizing the outcome of a non-biological system comprising a single-digit number of components can successfully rely on mathematics. But this is virtually impossible if one deals with biological systems, due to their random complexity and indeterminacy. In fact, it is precisely their inherent indeterminacy that explains the adequacy of evolution for the task of optimizing their efficiency. Thus, current biology finds itself in a curious position. It enjoys increasing analytical power arising from sophisticated tools and techniques, but it frequently appears unaware of the crucial distinction between simple and complex systems. (As a result, the explanatory limits of ontological reductionism are often underestimated by scholars of different branches of biology.) A concept advanced in this essay is that the smallest entity that can be meaningful to a biologist is what theoreticians of cybernetics and information theory have long referred to as a ‘system’, an entity exhibiting goal-seeking behavior, regulation and communication capacities, properties that the nineteenth-century supporters of vitalism had ultimately assigned to an “élan vital.” These properties become self-evident only when the various elements of a system are combined together according to their information processing capacities, in such a way that they end up by serving a higher-level entity. Eventually, it is such a higher-level entity that exhibits emergent properties. I finally hypothesize that it is a multidimensional topology of ‘functional fractals’ that allows living systems to handle large amounts of information, thereby responding efficiently to the technical challenges imposed by the environment. These functional entities might be distinguished according to both the type of information they handle and their information-processing abilities, and will determine the functioning of an entire organism on the basis of their self-organizing capacities.

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Building quantitative understanding of an embryo as it builds Itself

The ultimate computer simulation of embryogenesis will start from a fertilized egg and produce the next generation as another simulated fertilized egg. In between are all the events of embryogenesis and the life of the organism. This research program is likely to take a few generations of scientists. To start it off we begin at the simplest place for a physicist (“Given a spherical cow”…), with the physical properties of the fertilized egg. Because they are bigger, we use axolotl eggs, and will show what progress we have made in understanding cortical rotation, which occurs before first cleavage, and defines left/right and head/tail. As the embryo divides into many cells, differentiation waves appear to determine which cells become which kinds at given times, and thus represent the physical component of the genetic program for cell differentiation. We propose that a more general mechanism then sets in involving coordination between two cytoskeleton based signal transduction mechanisms based on microtubules and microfilaments.

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Measurement, morphology and mechanism: Why developmental biology needs morphometrics

In evolutionary biology, the need for morphometrics has grown naturally out of a focus on phenotypic diversity within and among species and also out of the appreciation of and interest in variation that is foundational to evolutionary theory. This is not true for developmental biology. In the past, the central questions of developmental biology have centered on how organisms develop. Variation in development was of secondary interest to questions about the causes of the major morphological and physiological transformations that occur in the development of particular model organisms or humans. With the rise of molecular techniques, the central questions of development have moved further from the study of phenotypic variation, revolving instead around the developmental-genetic pathways that underlie developmental processes. I argue in this essay that the study of variation, both in processes and morphological outcomes of those processes, is critical to developmental biology both to bridge the gap between developmental and evolutionary biology and also to understand the developmental and genetic basis for etiologically complex developmental malformations. Morphometrics will play a key role in this coming synthesis.

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Bio-chemometrics: Finding dynamics and harmonics in the cacophony of data from molecular biology

Modern biology represents a fertile meeting ground for different scientific cultures. My own research combines inductive and deductive research approaches, by "soft" data-driven modeling and "hard" theory-driven modeling, respectively.
My own scientific field, chemometrics, was traditionally concerned with how to design investigations to ensure informative data, how to extract relevant and reliable main information from large data tables by multivariate "soft" data-driven modeling in latent variables, and how to validate and interpret the modeling results.
In our research groups we now deal with new challenges arising when the bio-related fields of laboratory robotics, bio-spectroscopy, animal nutrition, breeding genetics, functional genomics and systems biology meet: How to deal with megavariate (instead of multivariate) complexity? How to interpret unknown high-dimensional non-linear dynamic systems with feedback, in light of background knowledge? In our search for causal insight in complex real-world systems, we combine mechanistic differential equation systems, computational statistics, chemometrics, computer science, and cognitive science.

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HUMAN SENSES IN ACTION: Multivariate measurements of quality

In this lecture I shall reflect upon quantification in biology, in two ways. First, from a sensory scientific perspective, addressing theories and methods for studying sensation, perception, and cognition as an information-processing system. Sensory science concerns action of the human senses such as sight, smell, taste, touch and hearing. The senses are not passive receivers but operate in an active and fundamental way for human beings in various social and environmental contexts. By biological senses we measure biology. In the past we could handle one-to-one relationships within a univariate frame. Today we have tools and thoughts to capture complexity closer to real-world situations. Thus, the second perspective is rooted in multivariate thinking and modeling tools. Mainly relying on soft modeling, explorative methods, such as partial least squares regression (PLSR), I claim that quantification in biology today enables future challenges to be met with a dialectic view of the process of exploiting the two perspectives simultaneously. Two examples will illustrate this, one showing perception of beer quality as an identity marker, the other addressing how sensory methods can be used to reveal a sensory morphological wheel that biologically describes cell differentiation by using PLSR.

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The unreasonable ineffectiveness of Fisherian statistical methods in biology and especially medicine

Medicine and epidemiology are doing damage with Student's t. The scale along which one would measure oomph is clear in medicine: Life or death. Cardiovascular epidemiology, to take one example, combines with gusto the fallacy of the transposed conditional and the sizeless stare of statistical significance. Some medical editors have battled against the 5% philosophy. Kenneth Rothman, the founder of Epidemiology, forced change in his journal, but only his journal. Decades ago a sensible few in education, ecology, and sociology initiated a "significance test controversy." But grantors, journal referees, and tenure committees in the statistical sciences had faith that probability spaces can judge - the "judgment" merely that $p < .05$ is "better" for variable X than $p < .11$ for variable Y. It is not. It depends on the oomph of X and Y, the effect size in view of how much it matters for scientific or clinical purposes. In 1995 a Cancer Trialists' Collaborative Group came to a rare consensus on effect size: ten different studies agreed that a certain drug for treating prostate cancer can increase patient survival by 12%. An eleventh study published in the New England Journal dismissed the drug. The dismissal was based not on effect size bounded by confidence intervals based on what Gosset (the "Student" of Student's t) called "real" error.

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The concept of morphospaces in evolutionary and developmental biology

Mathematical spaces have become commonplace conceptual and computational tools in a large array of scientific disciplines, including both the natural and the social sciences. Morphological spaces, or morphospaces, are spaces describing and relating organismal phenotypes. They play central roles in classical and modern approaches to morphometrics, the statistical description of biological forms, but also underlie the notion of adaptive landscapes that drives many theoretical considerations in evolutionary biology.
I will briefly review the topological properties of the most common morphospaces in the biological literature. In contemporary geometric morphometrics, the notion of a morphospace is based on the Euclidean tangent space to Kendall's shape space, which is a Riemannian manifold. Many more classical morphospaces, such as Raup's famous space of coiled shells, lack these metric properties, e.g., due to arbitrary scales of the variables, so that such morphospaces usually are affine vector spaces. Other notions of a morphospace, like Thomas and Reif's skeleton space, do not a give rise to a quantitative measure of similarity at all and constitute topological or pre-topological spaces.
The typical language of theoretical and evolutionary biology, comprising statements about the "distance" among phenotypes in an according space or about different "directions" of evolution, is not warranted for all types of morphospaces. In general, the larger the phenotypic variation that a morphospace should encompass, the less stringent are the geometric properties of this space. However, graphical visualizations of morphospaces or of adaptive landscapes may tempt the reader to apply "Euclidean intuitions" to a morphospace, whatever its actual topology might be. I discuss the limits of metaphors such as the developmental hourglass and macroevolutionary adaptive landscapes that ensue from the geometric properties of the underlying morphospace.

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Numbers and quantification: Where do they come from?

We humans have created numbers and quantification as tools for making sense of the world we live in. These conceptual entities, playing a fundamental role in mathematics, provide precision, true inferences, and objectivity in the quest for understanding nature. But, how can we evaluate "Truth" when purely imaginary entities are concerned? And how can we "objectively" share imaginary entities with others in a stable and consistent way? Mathematics provides a very intriguing case for studying these questions. Indeed, mathematics on the one hand deals with purely imaginary entities (e.g., a Euclidean point has only location, but no extension), and on the other hand, it provides extremely stable patterns of true-valued inferences (i.e., theorems) that once proved, stay proved forever (e.g., the

Pythagorean Theorem). In this talk I will analyze these issues by looking at both, my own work (with George Lakoff) on the Cognitive Science of Mathematics, as well as my field work in the Andes' highlands studying, with convergent linguistic-gestural-ethnographic methods, a very peculiar form of spatial construal of time in the Aymara culture. I will address the question of the role of axiom systems, and will show that the nature of Truth and Objectivity in abstract conceptual systems (e.g., number systems) hinge on the intricacies of the underlying human cognitive mechanisms (e.g., conceptual metaphors, metonymies, blends) that make them possible.

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Biology certainly needs morphometrics: Does morphometrics need biology?

It is now well documented that geometric morphometrics can provide useful and often unexpected information about anatomical forms relating to development and growth, functional especially mechanical adaptations, and evolutionary differences and relationships. However, further consideration of the biological determinants of anatomical landmarks implies that new mathematical treatments may need to be imported into geometric morphometrics. Perhaps anatomical features are not just individual landmarks but exist within concentric functional shells that require more complex morphometric treatment.

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Psychomorphospace—from biology to perception, and back: Towards an integrated quantification of facial form and function

Several disciplines share an interest in the evolutionary forces and constraints that shaped and continue to shape our minds, our behaviors, and our bodies inside and out. Traditionally, disciplines studying these processes address one domain at a time. The conceptionalizations and methodologies invoked by those disciplines often are conflicting and based on different explanatory rhetorics, hampering progress in one field from effective transfer to and adoption by the other. Topics at the intersection of anthropometry and psychometry, such as the impact of sexual selection on the hominin face, are a typical example. Yet, as the underlying (evolutionary) theory explicitly places facial form in the middle of a causal chain as the mediating variable between biological causes and psychological effects, a particularly convenient conceptual and analytic scenario arises: Modern morphometrics allow regressing shape both “backwards” on biology, and “forwards” on behavior/perception. These effects can be compared and evaluated as directions in the same morphospace. We suggest exploiting evolutionary aesthetics in toto in this space, where psychological and other processes of interest can be jointly encoded. Such a translation permits us to study and relate the effects of biological processes on form to the perceptions of the same processes in one “psychomorphospace.”
