Structure-function relationships revisited

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RS-B
Reflexive Systems Biology

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Reflexive Systems Biology

Towards an Appreciation of Biological, Scientific and Ethical Complexity

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RSB Reflexive Systems Biology

Summary: The ambitions of systems biology and synthetic biology are often stated in terms of prediction, control, design and fabrication of organisms. If possible, the ethical and social aspects involved would be huge, including those of biosafety and biosecurity. We propose an advanced project combining Science and Technology Studies with theoretical biology/ complexity theory in order to clarify and assess the ambitions of systems biology and their implications. This will be achieved by an interdisciplinary dialogue approach across the natural and social sciences. In this way, the project will be a contribution to a socially robust systems biology, in which scientific practitioners develop and act upon a reflexive understanding of their own role.

Reflexive Systems Biology: Work Plan

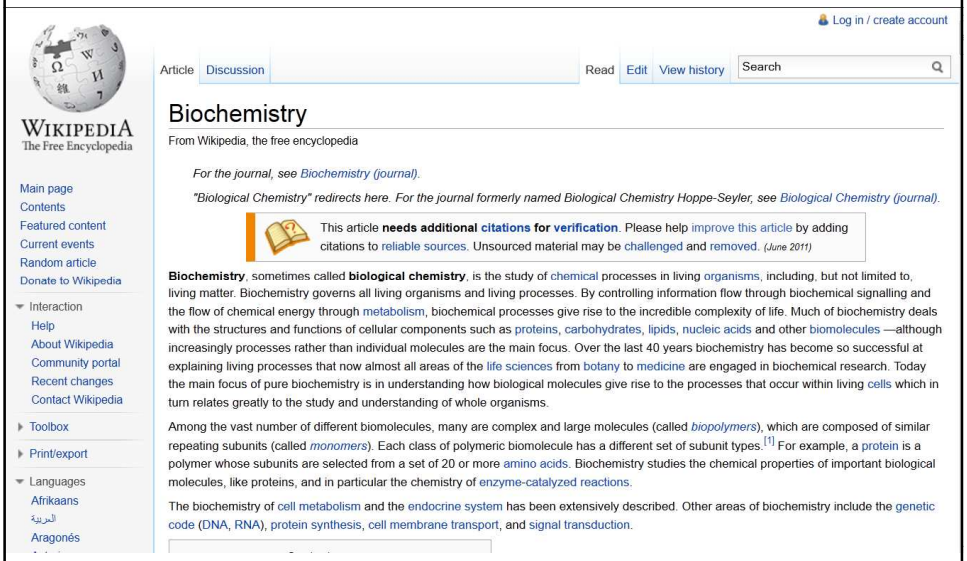
1. Overview of **existing types of designs/ formalizations** ("grammars") of theoretical models in systems biology.
2. Overview of currently recognised **possible future designs**.
3. Assessment of the potential and limitations of the designs.
4. Mapping of the perceived potential and limitations with respect to long-term future **knowledge and technology outputs**, including the prospects of design and **fabrication of life forms**.
5. STS **description** of systems biology that couples the complexity of the organism, with the complexity of scientific practice.
6. A mapping of potential **ethical and social aspects**.
7. Recommendations for **policy and governance**.
8. De facto **midstream modulation** of research practice
   a. by developing the results in 4-7
   b. by exploring whether and how they are to be accounted for in our life science partners' on-going research practice.

Structure-function revisited

- Biochemistry
- Systems biology
  - *Computational biology*
  - *Omics-driven systems biology*
  - *Relational biology (Robert Rosen)*

- *– Boundaries defining objects are to some extent arbitrary.* (John Dupré 18 Oct)
- *– Arbitrary, but immensely significant.* (Fern Wickson 18 Oct)
- How to analyse the choice of boundaries?

Biochemistry



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Biochemistry

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For the journal, see Biochemistry (journal).

"Biological Chemistry" redirects here. For the journal formerly named Biological Chemistry Hoppe-Seyler, see Biological Chemistry (journal).

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Biochemistry, sometimes called **biological chemistry**, is the study of chemical processes in living organisms, including, but not limited to, living matter. Biochemistry governs all living organisms and living processes. By controlling information flow through biochemical signalling and the flow of chemical energy through metabolism, biochemical processes give rise to the incredible complexity of life. Much of biochemistry deals with the structures and functions of cellular components such as proteins, carbohydrates, lipids, nucleic acids and other biomolecules —although increasingly processes rather than individual molecules are the main focus. Over the last 40 years biochemistry has become so successful at explaining living processes that now almost all areas of the life sciences from botany to medicine are engaged in biochemical research. Today the main focus of pure biochemistry is in understanding how biological molecules give rise to the processes that occur within living cells which in turn relates greatly to the study and understanding of whole organisms.

Among the vast number of different biomolecules, many are complex and large molecules (called *biopolymers*), which are composed of similar repeating subunits (called *monomers*). Each class of polymeric biomolecule has a different set of subunit types.[1] For example, a protein is a polymer whose subunits are selected from a set of 20 or more amino acids. Biochemistry studies the chemical properties of important biological molecules, like proteins, and in particular the chemistry of enzyme-catalyzed reactions.

The biochemistry of cell metabolism and the endocrine system has been extensively described. Other areas of biochemistry include the genetic code (DNA, RNA), protein synthesis, cell membrane transport, and signal transduction.

Main page
Contents
Featured content
Current events
Random article
Donate to Wikipedia

Interaction
Help
About Wikipedia
Community portal
Recent changes
Contact Wikipedia

Toolbox

Print/export

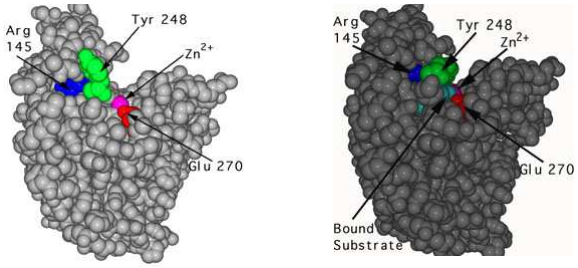
Languages
Afrikaans
العربية
Aragonés

Causal claims in Biochemistry

- Difference-making
  - Example: Phenylketonuria (Følling's disease)
  - PKU mutation → changed structure of phenylalanine hydroxylase (PAH) → impaired PAH activity → → → disease
- Production; Mechanism (in a non-philosophical sense)

Causal claims in Biochemistry

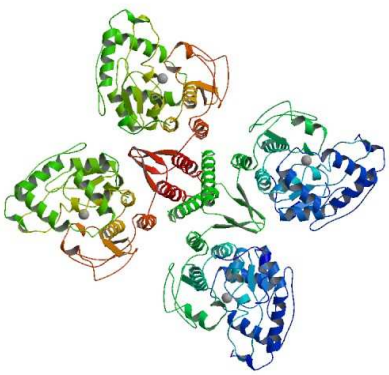
- Mechanism (in a non-philosophical sense): Structure accounts for function

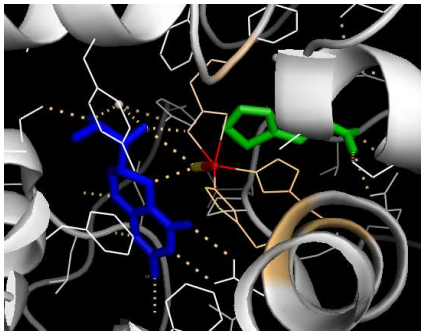


http://www.chemistry.wustl.edu/~edudev/LabTutorials/Carboxypeptidase/carboxypeptidase.html

Causal claims in Biochemistry

- Mechanism (in a non-philosophical sense): Detailed structure accounts for function





Causal claims in Biochemistry

- Difference-making
- Mechanism

- *– All attempts to understand causes must necessarily involve an observation of variation. Therefore biologists deliberately introduce perturbations.* (Elena Rocca, 19 Oct)
  - … also to simplify, idealize, allow for measurement (the in vivo-in vitro problem)
- However, mechanism is more than keeping track of differences: biological function is thought to be determined/explained/accounted for by structure (a type of reductive physicalism)
- I.e., the scientific *concept* of a mechanism goes beyond the data

From old to new

- One structure displays many functions
- Many structures involved in one function
- Severe context-dependency
  - The Nore-Mumford/Anjum debate: either the list of dispositions of X becomes indefinite, or it changes with context
- Imperfect prediction

Systems biology as an answer

- One structure displays many functions; Many structures involved in one function; Severe context-dependency; Imperfect prediction

- ***Responses:***
- *Massive measurement of multivariate data; book-keeping of correlations («omics»)*
- *Some simple structure-function relationships in «full quantitative detail» (chemical biology, computational biology)*
- *Massive sets of dynamic equations (or simplified sets (Westerhoff))*
- *Relational biology (Rosen): choosing functions and not structures as units of analysis*

The inevitable trade-offs

- «Full quantitative detail» in mechanism requires simple and/or idealized systems: no context sensitivity
- Omics is simply massive difference-making: no mechanism
- Relational biology: nobody ever understood how to make it into empirical research

- *– Boundaries defining objects are to some extent arbitrary.* (John Dupré 18 Oct)
- *– Arbitrary, but immensely significant.* (Fern Wickson 18 Oct)

Knowledge and Power come to the same thing

> Providing an explanation is, in a nutshell, working at empire-building; the more powerful an explanation, the larger the empire and the stronger the material in which it is built. What we admire in powerful theories we should also admire in freeways, multinational corporations, satellite networks, weapon systems, international banking and data banks. If we do not admire these achievements, there is no basis for using a double standard and letting the 'powerful theories' stand apart and alone be worshipped.

Bruno Latour (1988): *The Politics of Explanation*

Technoscience

- Production
  - Making things in industrial systems
  - Improving efficiency by removing context variability *(«The Pasteurization of France»)*
- Difference-making
  - To improve the population value of a certain function (e.g. health-related)
  - Artificial selection (human and non-human)
  - Intervening on human behaviour (standardizing)

Technoscience

- Technoscience is an activity that involves researchers and natural objects
- Techne: The world is acted upon (production, difference-making)
- Science: Narratives are made, cleansed from the active part of the researchers:
  - «The natural world is like this» «Mutation in the PAH gene causes PKU» «Enzyme X has 4 catalytic activities» «Afroamericans have lower IQ»
  - Work of purification: Hence technoscience is claimed to be morally and politically neutral and innocent.
  - Some philosophers buy into these narratives and think that it is their task to refine them even further.