Is there more to life than physics?

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This is a talk I gave at an ASU Faculty Club Colloquium (4/27/04) for a general audience. It addresses the conflicting "reductionist" and "animist" views of biology.

I begin by using Bohr's theory of the atom to illustrate the power of quantitative science. I then outline the prevailing theory of biology (natural selection) as an example of an "emergent phenomenon". I then turn to the simplest example of a biological machine – a protease, an enzyme that digests proteins, and show how it exploits random fluctuations by selecting those that drive the desired electron transfer reaction. In other words, the protease, and Darwin's finches operate by similar mechanisms!

Further examples of emergent phenomena that act like natural selection are: Molecular motors, the possible role of fluctuations in gene expression in development, the immune system, and, finally, selection of proteins important in brain development.

I conclude that genomics, proteomics etc. will lead to a form of personalized, predictive medicine that is like quantum mechanics. It will predict the "expectation values" but *never* the exact outcome for individuals. In that sense, the popular perception of life as a non-physical phenomenon is correct and the reductionists are wrong.

Physics – The miracle of Quantitative Science

Experiments: Optical emission from gasses is quantized and fits this formula

$1/l = R_H(a^2 - k^2)/a^2k^2$ k is integer, $a \geq k$

where $R_H = 10{,}967{,}758.1 \pm 0.7\ m^{-1}$.

If electron momentum is quantized in units related to Planck's constant, then I calculate the formula above with

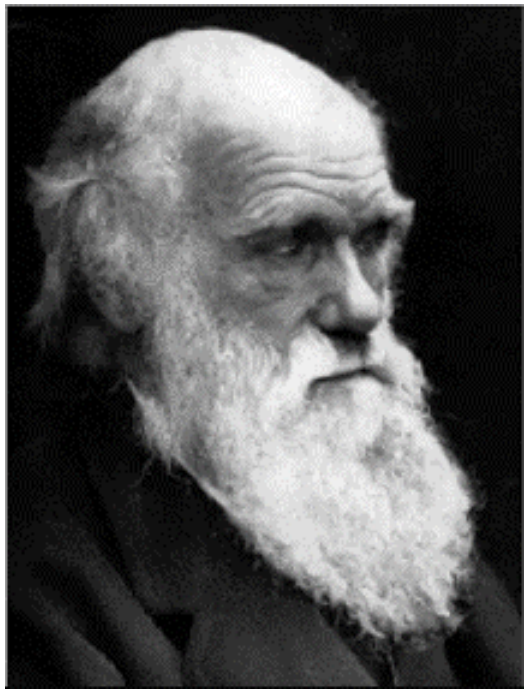
$R_H = me^4/8h^3\varepsilon_0{}^2c = 10{,}973{,}731.534\ m^{-1}$

Can these powerful methods explain life, or

Is there more to life than physics?

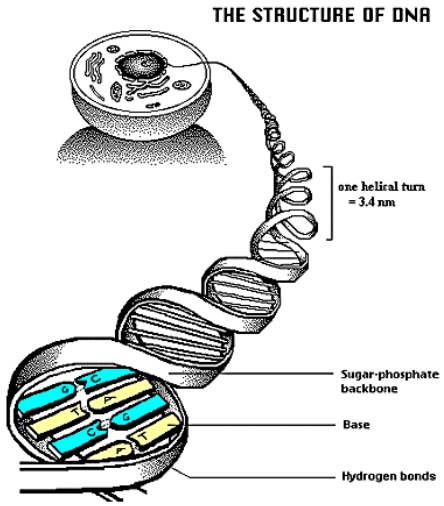
- Reductionist view:
  - Physicist: Everything is applied physics
  - Biologist: Now we have genome sequences, all is predictable
- "Popular/Religious" view: Living things are endowed with a "life force"

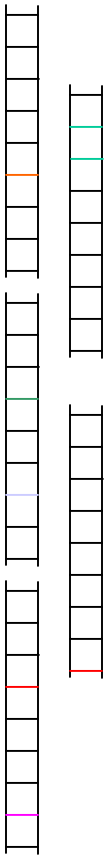
Population Biology – complex history driven by natural selection



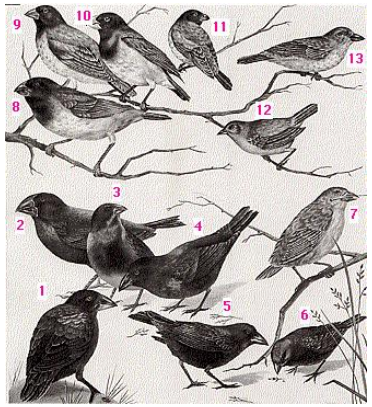
I have called this principle, by which each slight variation, if useful, is preserved, by the term Natural Selection.

Natural selection as an emergent phenomenon





Random DNA mutations



Random variation in phenotype

Selection:

The fit breed

Emergent Phenomena

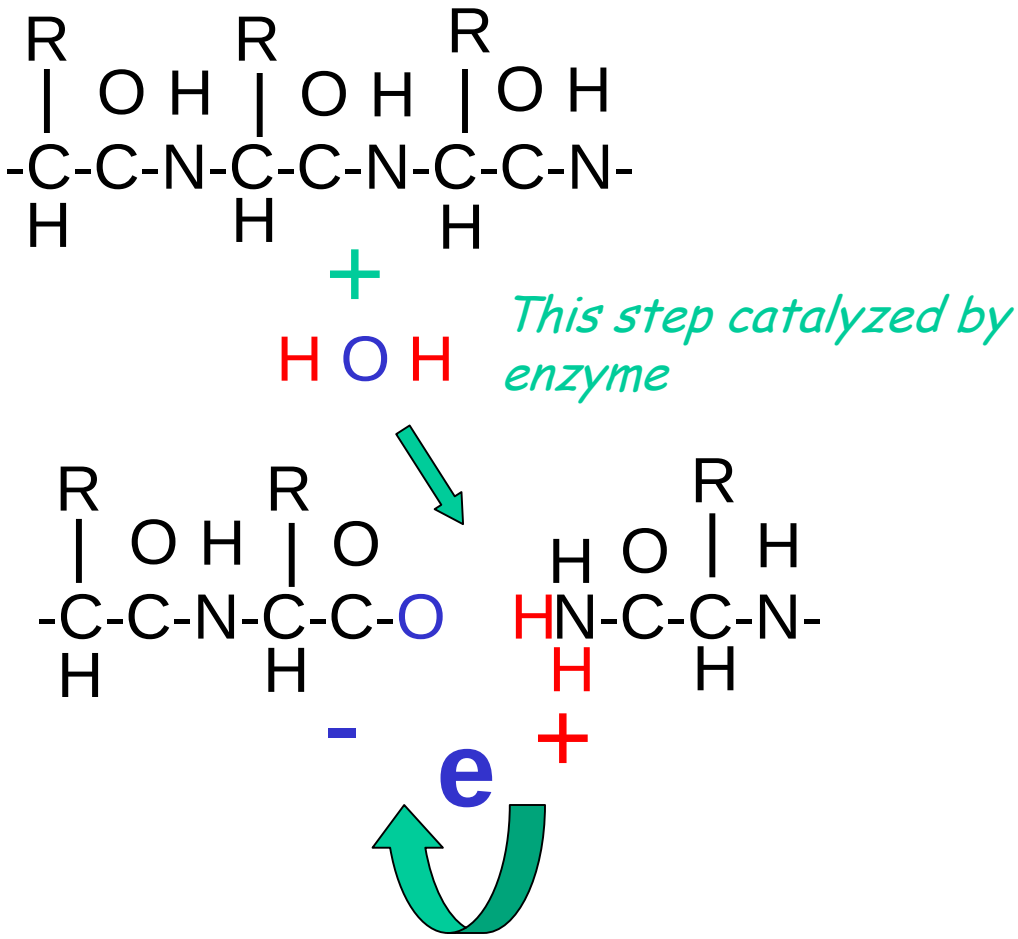
- Robust, simple principle you'd never guess from microscopic theory
- Independent of microscopic details
- Emerges in "complex" systems
- Examples: Evolution, Sound Waves

Is there a level at which Biology is not complex?

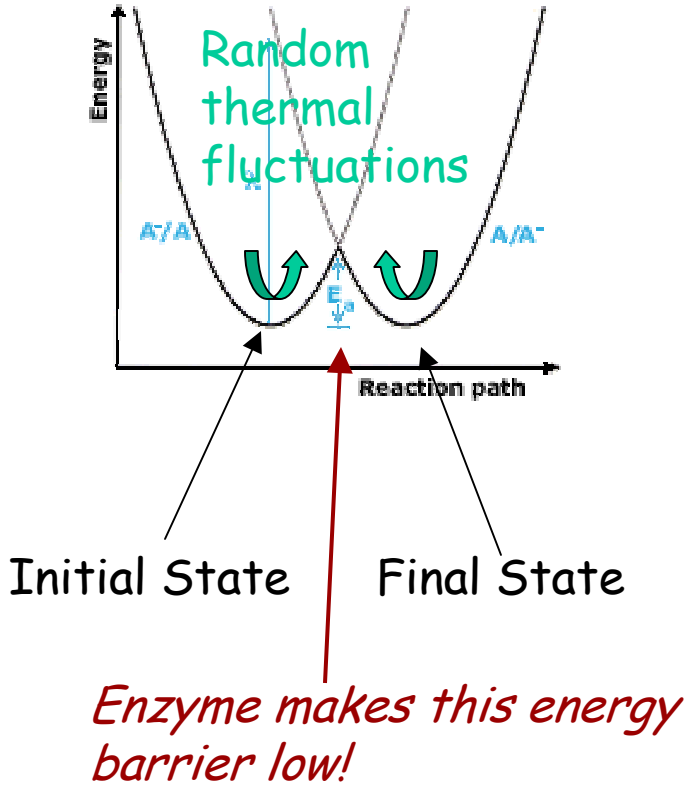
How about enzymes?

(Here comes the hard part…..)

Protease: eats proteins by peptide bind hydrolysis



Electron transfer reactions are driven by thermal fluctuations



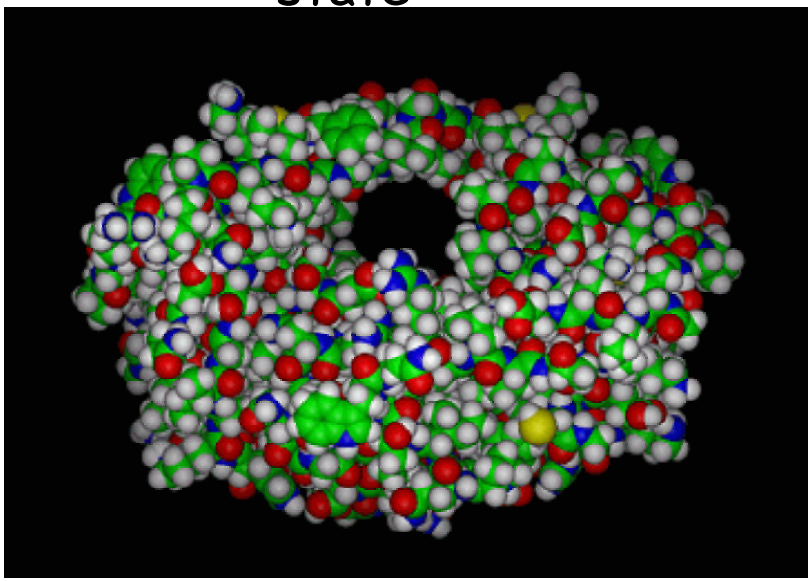
Enzyme catalysis as "Natural Selection"

Random structural fluctuations

Selection:

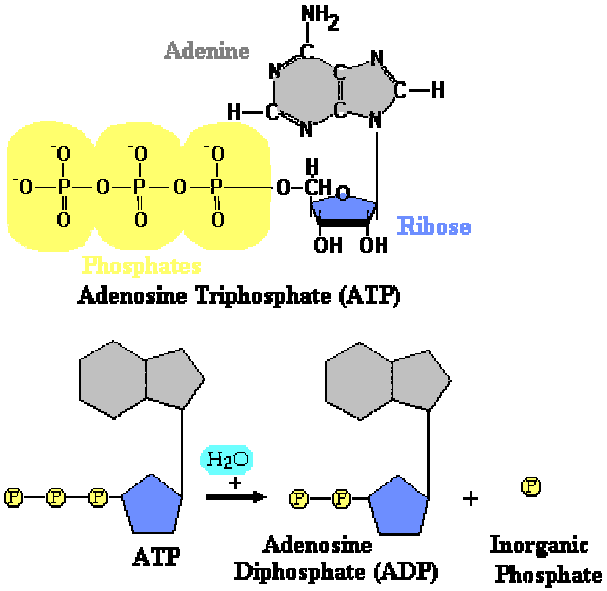
One fluctuation reaches the 'transition state'

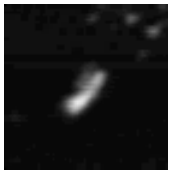
The bond breaks



Molecular Motors:

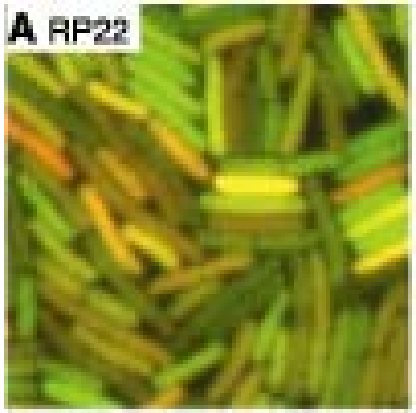
Random thermal motion biased by electron transfer reactions





Random fluctuation to transition state where ATP binding/hydrolysis drives step

Cell differentiation as a result of fluctuations?



Gene expression levels show 'few molecule' fluctuations

↓

Gene products regulate gene expression

↓

Therefore fluctuations can change phenotype

The Immune Response – Evolution in hours

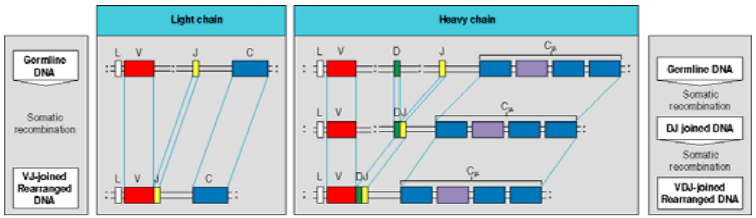
B Cells shuffle genes to make 'random' antibodies → "Right" antibody binds antigen → Right antibody cloned

Since there are multiple types of each gene segment, there are many thousands of possible V-D-J combinations so that each B cell gets a unique combination of segments! Additional diversity occurs because there are two types of light chains.

Number of functional gene segments in human immunoglobulin loci			
Segment	Light chains		Heavy chain
	κ	λ	H
Variable (V)	40	30	65
Diversity (D)	0	0	27
Joining (J)	5	4	6

Fig 4.3 © 2001 Garland Science

A unique recombination occurs in each B cell



- each B cell combines these gene segments to make an Ab chain like shuffling a deck of cards
  - V, D, and J are joined to C for the heavy chain, V and J are joined to C for the light chain

"Natural Selection" in Neuron Variability

Stochastic yet biased expression of multiple *Dscam* splice variants by individual cells

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The *Drosophila melanogaster* gene *Dscam* is essential for axon guidance and has 38,016 possible alternative splice forms. This diversity can potentially be used to distinguish cells. We analyzed the *Dscam* mRNA isoforms expressed by different cell types and individual cells. The choice of splice variants expressed is regulated both spatially and temporally. Different subtypes of photoreceptors express broad yet distinctive spectra of *Dscam* isoforms. Single-cell RT-PCR documented that individual cells express several different *Dscam* isoforms and allowed an estimation of the diversity that is present. For example, we estimate that each R3/R4 photoreceptor cell expresses 14–50 distinct mRNAs chosen from the spectrum of thousands of splice variants distinctive of its cell type. Thus, the *Dscam* repertoire of each cell is different from those of its neighbors, providing a potential mechanism for generating unique cell identity in the nervous system and elsewhere.

Is there a level at which Biology is not complex?

- If its not complex, its not biology
- Physical theories must capture source of randomness, selection rule
- Diversity is *ESSENTIAL*

So is Physical Science Useful in Biology?

- Modern computational capacity can capture and model the range of *diversity*
- At the molecular level only a few types of fluctuations may matter *and measurements are possible!*
- Can we work out 'predicitve' relationships between genotype and phenotype?
- Individual genotypes for $1000?
- Personal, predictive and preventative medicine?

Is there a level at which Physics is not complex?

The Theory of Everything

R. B. Laughlin and David Pines

Proceedings of the National Academy of Sciences 97, 28 (2000).

For the biologist, evolution and emergence are part of daily life. For many physicists, on the other hand, the transition from a reductionist approach may not be easy, but should, in the long run, prove highly satisfying.

Physics and Biology are becoming one…

- Information revolution in biology: we have the data!
- Complexity revolution in physics: we have the methods
- The *general* principles of biological machinary will be understood and the *overall* fate of individual organisms will become much more predictable BUT

Individual lives will remain forever mysterious and complex…