

Gratuity in Nature and Theology

Paul Arveson
American Scientific Affiliation
July 2006

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A talk given at the annual meeting of the American Scientific Affiliation, Calvin College, July 2006

(The rotating object is a model of the repressor protein that functions to control the *lac* operon.)

The Organism: *E. coli*



- The human colon contains billions of these bacteria
- Has built-in ability to adapt its “digestive system” to the kind of nutrient available (lactose, glucose, etc.)
- How does this work? – A major discovery in biology 40 years ago, with parallels in 4 other fields....

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In the early 1960's, shortly after the discovery of the structure of DNA, the so-called “secret of life” by Watson and Crick, molecular biology emerged as a new field of science. One of the common organisms studied was the bacterium *E. coli*. This organism has a built-in ability to adapt its metabolism, its digestive system, to the kind of sugars available in the environment. How does this work? This was a problem that has been studied since the 1930's.

The Discovery



Francois Jacob, Jacques Monod, Andre Lwoff

- ***“I have discovered the second secret of life!”***
 - Operon model
 - Allosteric proteins and gratuity
 - Paper published 1963
 - Won the Nobel Prize in Physiology in 1965 along with Jacob and Lwoff

One of the scientists working on this was the Frenchman Jacques Monod. Along with his colleagues Francois Jacob and Andre Lwoff, he won the Nobel Prize in Physiology in 1965 for two discoveries in particular: the operon model of control systems in the cell, and the description of what he called allosteric proteins and gratuity.



Francis Crick on Monod's Discoveries

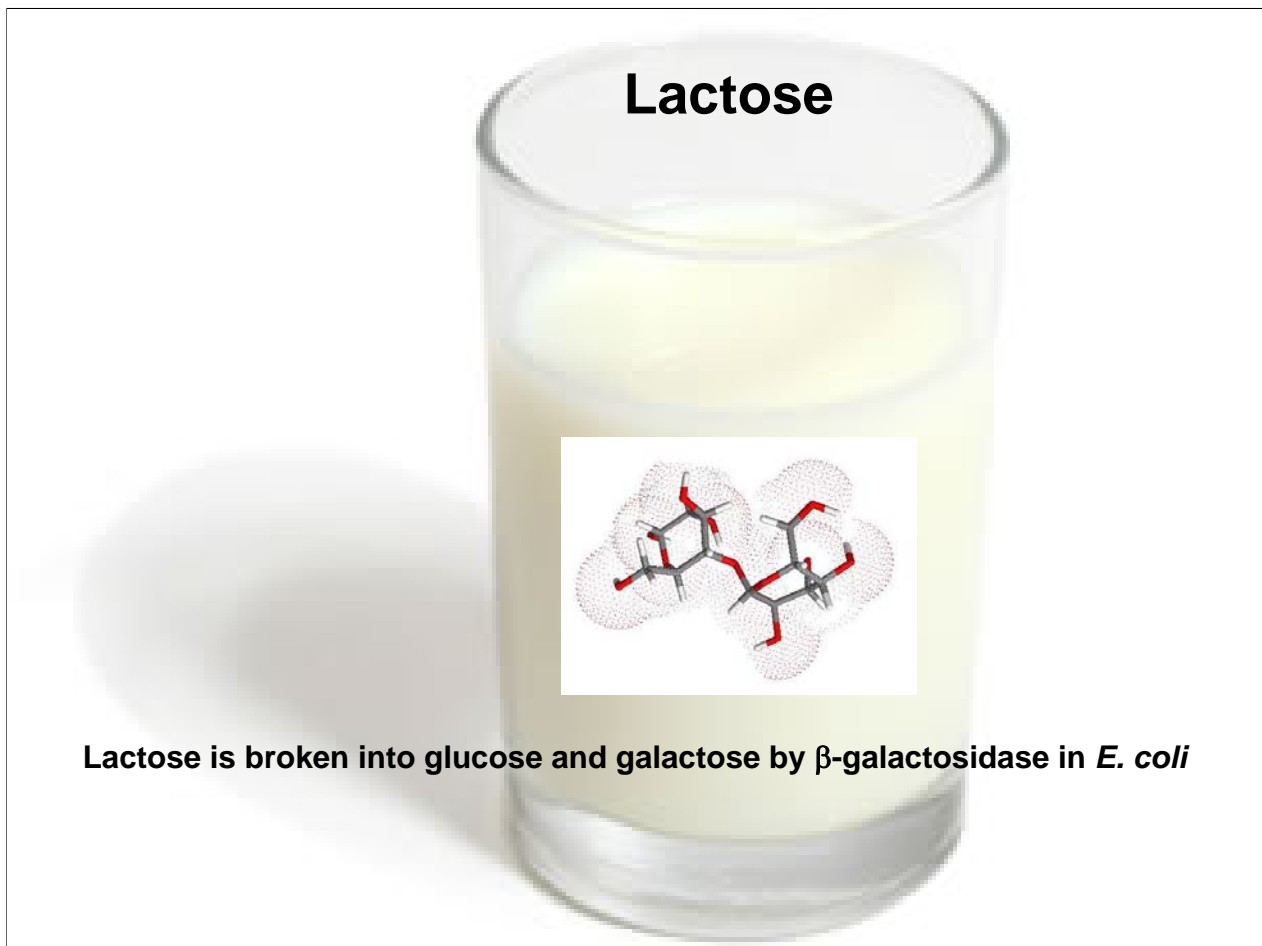
- Of all Monod's ideas, allostery was the one that Crick most admired. "I would say particularly, Jack Monod's work on allostery is a very powerful theoretical concept. Never mind the mechanism of it, which did have to be worked out [this was in 1971]. That meant that you could connect any metabolic circuit with any other metabolic circuit, you see, because there was no necessary relation between what was going on at the catalytic site and the control molecule that was coming in. Well, that's an extremely powerful idea, never mind the details."

Quoted in *The Eighth Day of Creation*, H.F. Judson, Simon & Schuster, 1979, p. 579

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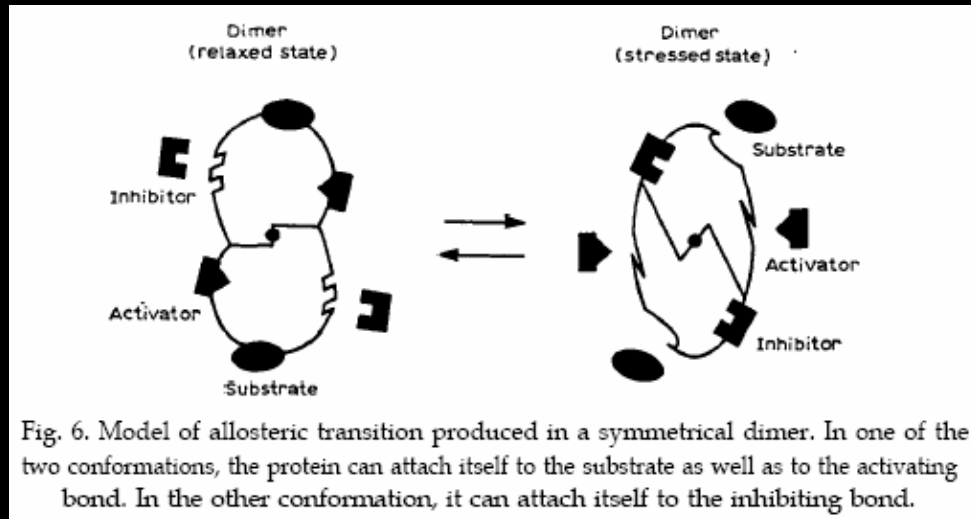
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Allostery refers to the fact that some enzymes contain more than one active site, unrelated to one another chemically. The prefix allo- means other or different.



Let's examine how this works with a common energy source, milk sugar or lactose. Lactose is broken down into two simpler sugars, glucose and galactose by β -galactosidase in *E. coli*. These are easier to metabolize by the cell. The process to adapt and break down lactose, which was described by Jacques Monod, is called the lac operon. This process is well understood now and is described in any molecular biology textbook.

Monod's Model of an Allosteric Enzyme



Jacques Monod, "From enzymatic adaptation to allosteric transitions", Nobel Lecture, 1965

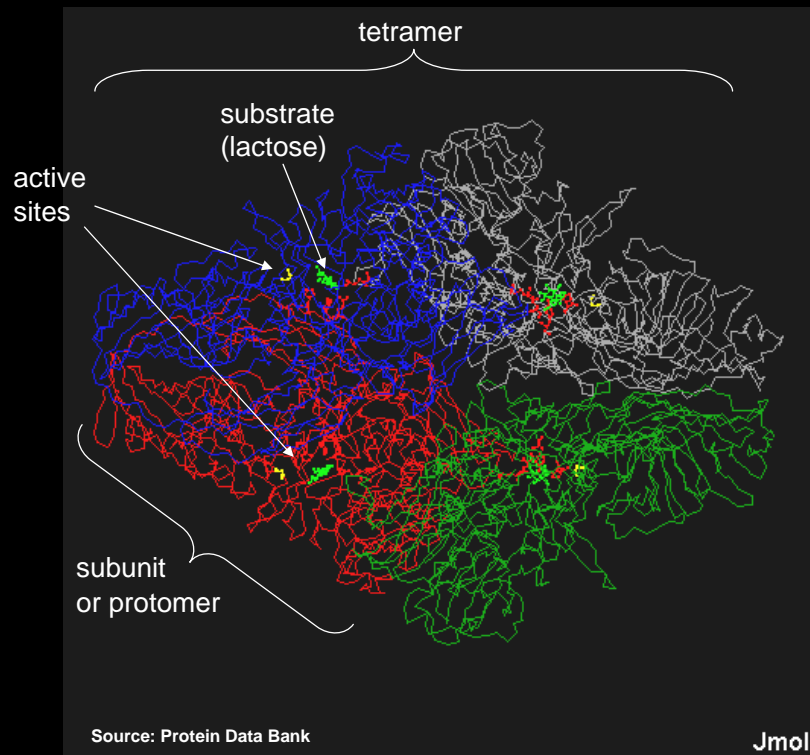
Monod presented this diagram that schematically illustrates the operation of an allosteric enzyme. It has two forms, relaxed and stressed or tensed, which have slightly different shapes. The shapes are in turn controlled by two other small molecules that can attach to the molecule at specific active sites, and they serve to either bind the substrate or release it. In our case the substrate is lactose.

β -galactosidase – lactose bound to active sites

β -galactosidase is an oligomeric allosteric enzyme. Here it is shown in its relaxed state, in complex with the substrate *d*-lactose.

There are four identical subunits assembled by noncovalent bonds, which act in concert.

The equilibrium between the relaxed and tensed states is a fourth power of the concentration of the ligands.

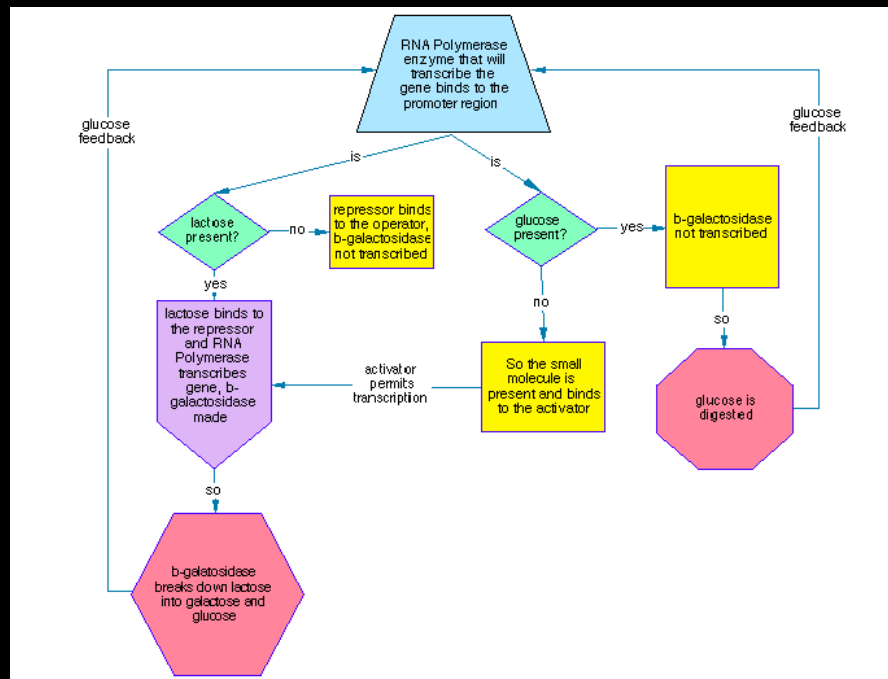


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Here is a modern wireframe model of the enzyme beta-galactosidase, which is an allosteric enzyme, from the Protein Data Bank. It is constructed of four identical subunits or protomers, which join together to form a tetramer. There are active sites on each of the subunits. This picture shows the complex of the enzyme with lactose bound in the active sites.

lac Operon Model as a Flowchart



http://www.scitv.com/welz/genome/welz_genome0.html

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The enzyme beta-galactosidase forms a component of a process that includes other enzymes and three genes in the DNA. This process is called the *lac* operon. Most of the figures that describe the operon model in textbooks and on the Internet are static drawings of a part of the process. They often are oversimplified and cannot show the dynamics of the process.

This figure, a traditional style flowchart, makes an attempt to include the dynamic character of the operon process. These processes occur in parallel, but the flowchart description does not restrict this. A “swim lane” flowchart would be even better and clearer. But this is the only such figure I could find on the Internet.

Anyway in this talk I only want to focus on the key component in this process, the allosteric enzyme and its underlying principle that Monod discovered.

What is Gratuity?

- Gratuity is the freedom from any chemical or structural necessity in the relation between the substrate of an enzyme and the other small molecules that prompted or inhibited its activity. "It has to be a system which has the basic property of an electronic system..." Allosteric proteins were relays, mediating interactions between compounds which themselves had no chemical affinity, and by that regulating the flux of energy and materials through the major system, while themselves requiring little energy. The gratuity of allosteric reactions all but transcended chemistry, to give molecular evolution a practically limitless field for biological elaboration.

Interview, J. Monod, 1 Dec. 1975, H.F. Judson, *The Eighth Day of Creation*, Simon & Schuster, 1979, p. 575

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What is gratuity? I'm just going to quote Monod or his interviewer directly on this subject:

Monod on Gratuity (1970)

- “There is no chemically necessary relationship between the fact that β -galactosidase hydrolyzes β -galactosides, and the fact that its biosynthesis is induced by the same compounds. Physiologically useful or “rational”, this relationship is chemically arbitrary – “gratuitous”, one may say.”

Jacques Monod, *Chance & Necessity*, 1970, ch. 4

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Monod on Gratuity (2)

- “From this it results – and we come to our essential point – that so far as regulation through allosteric interactions is concerned, *everything is possible*.... The way in which allosteric interactions work hence permits a complete freedom in the “choice” of controls. And these controls, having no chemical requirements to answer to, will be the more responsive to physiological requirements, and will accordingly be selected....”

Jacques Monod, *Chance & Necessity*, 1970, ch. 4

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Monod on Gratitude (3)

- “In a word, the very gratuitousness of these systems, giving molecular evolution a practically limitless field for exploration and experiment, enabled it to elaborate the huge network of cybernetic interconnections which makes each organism an autonomous functional unit, whose performances appear to **transcend the laws of chemistry** if not to ignore them altogether.”

Jacques Monod, *Chance & Necessity*, 1970, ch. 4

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When I first read Monod’s popular-level book *Chance and Necessity* back in the 1970’s, I was intrigued by this idea of gratitude, that seemed to have parallels in computer science and other fields. The term seems to have fallen somewhat into disuse. I eventually wrote an article about this, *Gratitude in Nature and Technology*, and here I am suggesting some applications of the concept to other fields.

Physicists Take on Biology (2006)

- *“Machines do not a cell make”*
 - Bias in knowledge of structure vs. function
 - Allosteric enzymes change their shapes
 - Dynamics are harder to visualize
 - Collective actions of many parts
 - Analogous to phonons in crystals
 - e.g. Ribosomes, transcriptosomes, proteasomes
 - A form of emergence
 - Nonequilibrium processes
 - Another form of “emergence”; chaos theory
 - Information feedback is often ignored

“The Biological Frontier of Physics”, R. Phillips & S. Quake, *Physics Today*, May 2006

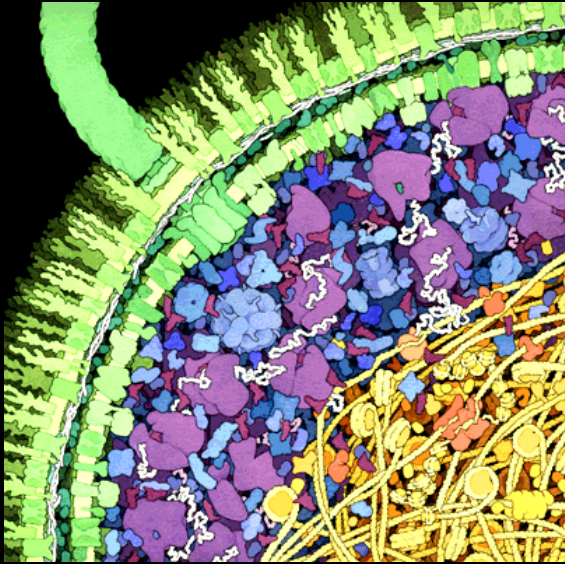
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Recently, some 40 years after the discovery of allosteric enzymes and gratuity, there has been an increased interest in applying some of the insights and discipline of physics to the study of life. The 21st century field of systems biology has really taken hold, with a clear agenda to bring various disciplines together to understand the dynamics of life.

Here are some critiques of biology levied by physicists in a recent issue of *Physics Today*.

Visualizing Cell Complexity



- “Cytoplasm” is a name for our ignorance
- Art by David Goodsell
- Still does not do justice to the additional complexity that has not yet been discovered but is probably there

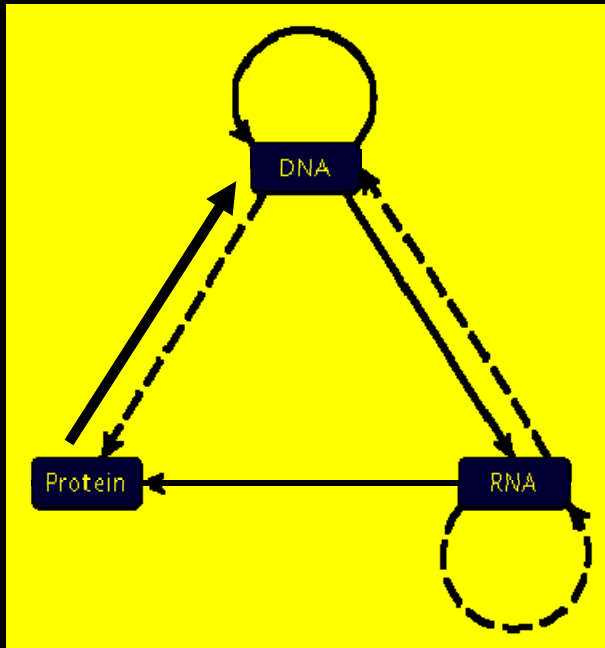
Source: David Goodsell, UCSD

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One bias that physicists noted is that we can only explain what we can visualize, and much of what goes on in a living cell cannot yet be visualized. Initially, all the material inside the cell was called “cytoplasm”. But even artists like David Goodsell cannot do justice to the range of 3D structures in the cell, much less the dynamic processes.

Information Feedback



- Central dogma as a “cartoon”
- Information also flows from proteins to DNA because proteins regulate the expression of genes (e.g. via operons)
- “Though all biologists know this; central dogma cartoons continue to omit the arrow that closes the loop.
- A closed loop in a formal theory would admit the possibility of feedback and complicated dynamics....

“The Biological Frontier of Physics”, R. Phillips & S. Quake, *Physics Today*, May 2006

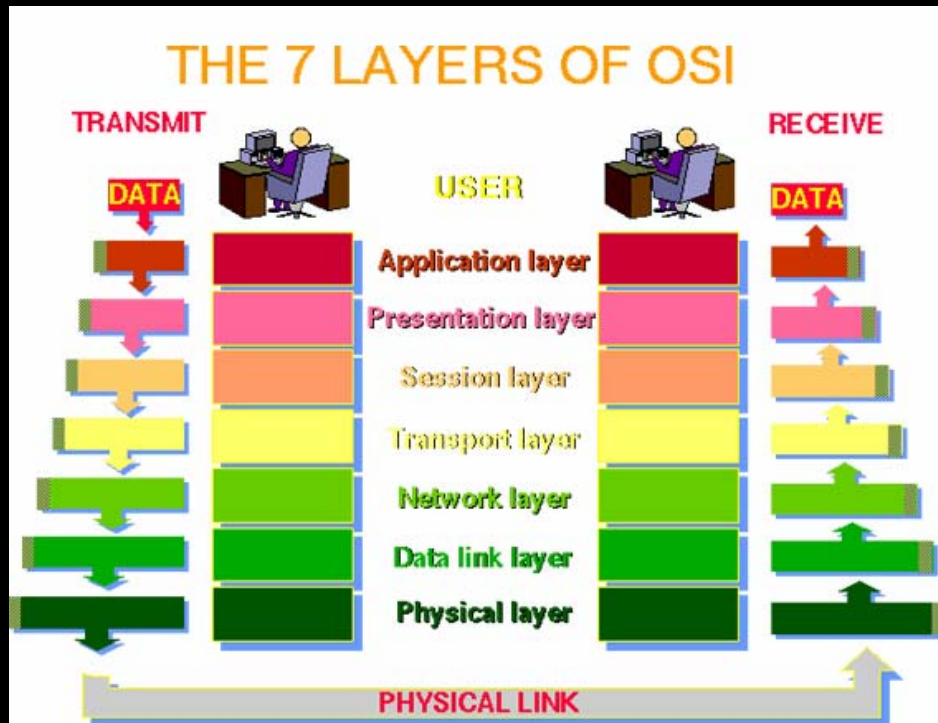
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Another one of the criticisms physicists levied on biologists is that often they draw dynamic processes as “cartoons” that do not accurately represent the whole picture. Here is the classic picture of the central dogma DNA → RNA → protein.

But in fact, as the operon model shows, there is also feedback from the proteins to DNA. This feedback loop opens up the whole system to a much greater range of possibilities.

Gratuity in Computer Network Technology



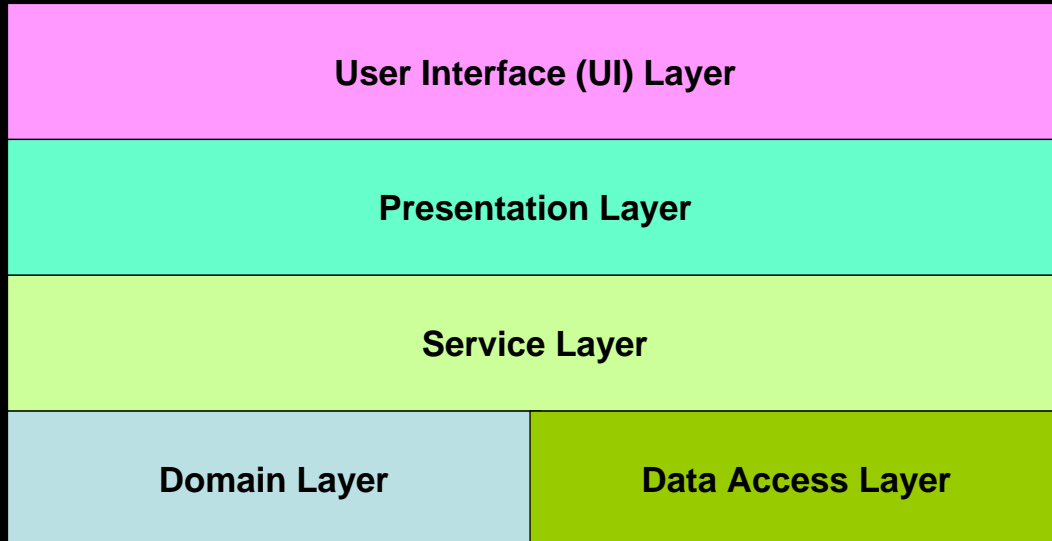
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In the earlier paper on Gratuity in Technology I followed Monod's example by comparing the operon to processes in electronic computers. Here we also see a principle of gratuity at work.

Computer networks like the Internet are able to transmit data over noisy, unreliable connections with very low error rates. At each layer, a small amount of control information is added to the message content before it is sent to the next layer. The data inside the message is not read; it may include a checksum for error checking but otherwise its content is irrelevant, only the control header is actually read, like the envelope of a letter. This represents a kind of gratuity in the relationship between the message and the control information.

Gratuity in Software Application Architecture



<http://msdn.microsoft.com/msdnmag/issues/06/08/DesignPatterns/default.aspx>

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Here is another example of gratuity from software engineering. This figure shows the main layers that make up a typical application. I'm just going to quote from the article that described this figure:

“Notice that there are separate packages for UI and presentation. You might have expected them to be the same, but actually the UI layer of a project should consist only of the various UI elements—forms and controls.

Why is it bad to have lots of logic in the UI layer? The code in the UI layer of an application is very difficult to test without either running the application manually or maintaining ugly UI runner scripts that automate the execution of UI components. While this is a big problem in itself, an even bigger problem is the reams of code that are duplicated between common views in an application. It can often be hard to see good candidates for refactoring when the logic to perform a specific business function is copied among different pieces in the UI layer. The MVP design pattern makes it much easier to factor logic and code out of the UI layer for more streamlined, reusable code that's easier to test.”

Computer Technology Translated into Biological Terms

Protein Layer
RNA Layer
DNA Layer

- “Why is it bad for cells to simply follow the central dogma: DNA -> RNA -> protein? The sequence of DNA would have a difficult time fixing errors or evolving. While this is a big problem in itself, an even bigger problem is the excessive number of residues that would have to be duplicated for similar functions in a cell. The operon model makes it much easier to reduce the amount of protein that must be manufactured for respiration and metabolism.”

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Now I'm going to make a (rough) translation of this language of software to the biological description:

This kind of “systems biology” approach I think has a lot of potential; by bringing together systems from various fields and looking for similarities that can help in understanding nature. The Santa Fe Institute was a pioneer in this approach, and now many schools and institutes have grown up around this field. It is much more sophisticated and, I believe, more likely to succeed than the early approach of “General Systems Theory”.



“We are all reductionists now”?

- “Is it really true that there are new kinds of laws that govern complex systems?”
- “....We would not pay much attention to a proposed autonomous law of macroeconomics that could not possibly be explained in terms of the behavior of individuals or to a hypothesis about superconductivity that could not possibly be explained in terms of the properties of electrons and photons and nuclei.
- The reductionist attitude provides a useful filter that saves scientists in all fields from wasting their time on ideas that are not worth pursuing.
- In this sense, **we are all reductionists now.**”
 - Stephen Weinberg, *Dreams of a Final Theory*, Vintage, 1994, p. 64.

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Systems biology still faces the challenge of reductionism. 20th century physics is built upon two fundamental types of entities: particles and fields. With these two entities alone, physics has been able to construct the Standard Model, a description of the entire universe, from small to large, that has, in principle at least, reduced every phenomenon to three fundamental forces and a few remaining free parameters.

The Standard Model can predict some of the properties of particles to 11 decimal places of precision. It represents the triumph of reductionism, and now physicists like Stephen Weinberg dream of a final “theory of everything.”

Here is Weinberg’s objection to non-reductionist views of systems:

Earlier Non-Reductionist Views that were Rejected by Monod

- Miracles, Cartesian dualism, etc.
- Dialectical materialism –Engels, Lamarck
- Metaphysical vitalism - Bergson
- “Scientistic vitalism” - Driesch, Elsasser, Polanyi
- “Animism” - Leibniz, Hegel, Teilhard de Chardin
- “Scientistic progressism”
- “Anthropocentrism”

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Those who would propose non-reductionist views should beware that Monod may not be sympathetic. In his day there were a variety of them that he dismissed with scorn in *Chance and Necessity*.

For instance, I think that Monod and the other biologists of his time were successful in finally completely driving vitalist views out of science.

Current Non-Reductionisms

- **Special Creationism**
 - Insistence that special interventions were necessary to form every kind of living thing.
- **Eastern metaphysical monism, pagan holism**
 - “All is one, and you are God”
 - “Everything is connected to everything else.”
- **Intelligent Design**
 - Insistence that there are gaps in life that cannot be explained by physical processes; they are “irreducibly complex”.
- **Non-reductive physicalism**
 - All processes are physical, but also give rise to “higher” human capacities such as morality and spirituality.
- **Critical realism**
 - Different levels of reality exist in an ontological sense.

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Here are four currently prevalent non-reductionist views of nature. Of course special creationism and Eastern monism are not new to us.

Intelligent Design is relatively new and is pertinent to our discussion. ID insists that there are gaps in life that cannot be explained by physical processes; they are “irreducibly complex”.

Where I differ with ID is that I am more optimistic that we can find physical explanations of biological structures and processes, gratuity being one of the clues.

I'll have some more to say about the last two views.



Strata in Human Nature

- **“Non-reductive physicalism”** sees cognitive capacities as emergent in the human species. Emergent properties appear as a result of a significant increase in some set of lower-level abilities, they cannot be totally accounted for in terms of the lower-level abilities.”
- “Soul” designates the person’s emergent property of capacity for personal relatedness.
 - Warren Brown, “Cognitive Contributions to the Soul”, in Brown, et al., ed., *Whatever Happened to the Soul*, Fortress Press, 1998

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“Non-reductive physicalism” sees cognitive capacities as emergent in the human species. Emergent properties appear as a result of a significant increase in some set of lower-level abilities, they cannot be totally accounted for in terms of the lower-level abilities.”

In this view the word “soul” designates the person’s emergent property of capacity for personal relatedness.

Non-reductive physicalism is of interest to many of us in ASA; in the symposium 2 years ago on Neuroscience Warren Brown described his view of brain function in terms familiar to computer scientists. NRP acknowledges, over against vitalisms, that the brain is entirely physical, but higher levels emerge in the brain’s functioning.



A Layered Reality: Roy Bhaskar's Critical Realism

- "...there has never been a route even from a highly developed lower-stratum science to a science with a higher-stratum object. Only when the latter is independently theorized can we begin to correlate the two, and perhaps explain the upper by the lower."
- [Furthermore], ... stratification is not grounded in contingent aspects of human cognitive capacities, but in a *real ontological stratification* of the object of the sciences. It is the real distinction between the strata and their irreducibility one to another which explain the distinctions between the various sciences....
- ".... for Bhaskar, the plurality of sciences is necessary because of the irreducibly stratified character of the mechanisms at work in the real world, so that the unity of nature is that of a laminate."

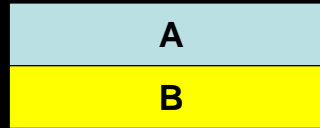
Collier, Andrew (1998). "Stratified Explanation and Marx's Conception of History", quoted in "Critical Realism, Essential Readings" ed. M. Archer et al., Routledge, London.

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The philosophy of critical realism was given a new lease on life by Roy Bhaskar in the last few decades. One feature of Bhaskar's view is his non-reductionist description of reality, and his argument claiming ontological standing for this description, that is, it is not merely a convenience or an epistemological question:

Meaning of the “Stratification of Reality”



- Roy Bhaskar argues that:
 - “Because level A is rooted in and emerges from level B, it does not follow that level A is therefore ‘nothing but’ level B. Emergent strata possess features that are ‘irreducible’”.
 - Reductionism to level B is therefore rejected.
 - This is a feature of the real world, not just a convenient way for humans to describe it.

In his books on Critical Realism, Roy Bhaskar argues that:

Note that these are philosophical claims, not demonstrations. They are more or less vague, qualitative statements. That’s why I am looking for examples and evidence for layered structure in the sciences, not just bare claims. Gratuity is one of the most dramatic examples of this stratification.



Theology and Stratified Reality

- “A stratified approach to reality allows the multi-leveled embeddedness of revelation in reality to be fully and thoroughly explored, and its impact on the maintenance of the Christian tradition to be identified.”
 - Alister McGrath (2004), *The Science of God*, Eerdmans, p. 151.

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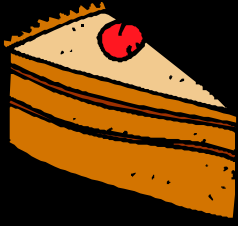
I was initially put on to Bhaskar by the British evangelical theologian Alister McGrath. There are several other British theologians who he says support critical realist views, including Ian Barbour, Arthur Peacocke, and John Polkinghorne.

Who ever thought that theologians would become more open-minded than physicists on these questions?

Tools for Understanding and Explanation

Field	Strengths	Weaknesses
Philosophy and theology: <i>seek understanding</i>	Relevant to human life; provides coherence; reveal logical fallacies; protect us from errors and deceptions.	Language abstract and vague; difficult to form unique interpretations and settled conclusions.
Physics: <i>seeks explanations</i>	Theories that are general enough for wide application; specific enough for measurements.	Doesn't address the big questions of life that humans desire most to know.
Traditional biology: <i>seeks solutions</i>	Practical; deals with vital information that can save lives and benefit the environment.	"Cartoons" and "stamp collecting" – too descriptive and specific; no deep understanding

Here is a very rough outline of the ways different fields of science have sought to understand reality in Western history.



On Matter

.... Where, then, is that person who ignorantly sneers at the study of matter as a material and gross study?"

-- Henry Rowland, Physicist, 1899

We are made of dust, but we may need new ways of seeing and thinking in order to understand the awesome things that God's dust can do.

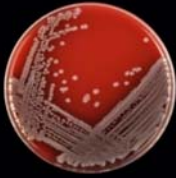
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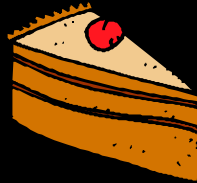
Here is an interesting quote by the physicist Henry Rowland at the end of the 19th century. He was the retiring President of the American Physical Society. After briefly describing some of the recent discoveries in atomic physics, he concluded in his speech:

The enemy of theology is not matter or materialism or physicalism; the Bible teaches that we are made of dust. The enemy comes from interpreting this humble nature as the only valid way to describe nature, i.e. reductionism. Gratitude indicates on the other hand the richness of God's dust.

Layers and Gratuity Evident in Many Fields



Biology



Physics



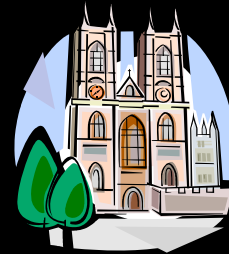
Human nature



Networks
& Software



Philosophy



Theology

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I have tried to show evidence of gratuity and layered descriptions of reality in many fields of knowledge. I do not mean to imply that all applications of gratuity are alike, nor are they all necessarily even valid. This is a very cursory review.

Hard Questions in Genetics

- How and Where Did Life on Earth Arise?
- How Far Can We Push Chemical Self-Assembly?
- What Determines Species Diversity?
- What Genetic Changes Made Us Uniquely Human?
- Why Do Humans Have So Few Genes?
- What Controls Organ Regeneration?
- Can We Selectively Shut Off Immune Responses?
- How Can a Skin Cell Become a Nerve Cell?
- How Does a Single Somatic Cell Become a Whole Plant?
- To What Extent Are Genetic Variation and Personal Health Linked?
- How Will Big Pictures Emerge From a Sea of Biological Data?

“Hard Questions”, *Science*, July 1, 2005

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Many hard questions remain to be explained, including many that relate to genetics and origins – according to mainstream scientists themselves.

Cognitive Barriers to Further Inquiry about the History of Life

- **Creationism** denies natural origins entirely, so for them there is no point in scientists' pursuit of a deeper understanding of life.
- **ID** claims that life contains systems that are intractable and we should give up, and simply attribute them to an "intelligent designer".
- Many **mainstream biologists** take life and evolution for granted, so they see no need to demonstrate them or explain them.
- **Physical reductionism** (to particles and fields) at least puts a cognitive stumbling-block in the way of further inquiry; at worst it could reflect a limited view of reality.

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All of these philosophies have the net effect of discouraging experimental inquiry or deeper human understanding of nature.

These are the same attitudes that Francis Bacon had to oppose in defending science at its beginnings in the 17th century.



Francis Bacon

One of the Conclusions

- **Biology is still young – it is likely that more fundamental discoveries like gratuity are just around the corner**
 - We are facing many hard questions, but it is the same *kind* of questions that science has faced many times before
 - Matter is a richer substrate than we generally think – dogmatic reductionism (to particles and fields) has narrowed our thinking
 - Many problems are multi-disciplinary and require insights from different fields (systems biology)
 - It is premature to give up and declare permanent gaps – *have a little more faith in science!*

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Here are some of the articles, books and web sites consulted for this talk.

Non-Reductive Physicalism May Offer a Balance between two Extremes

A: Non-Reductive: allows room for human life and meaning; interactions are not mere accidents. They are phenomena that can only be appropriately described in their own terms, on their own level. No field of science is in a position to dominate everyone else in an imperialist way, and take away their right to claim meaning and truth.

B: Physicalism: Matter is God's dust. It is a sufficiently rich substrate for all natural processes, with no need for miraculous or intelligent intervention. This is also consistent with van Till's notion of the competence of the original creation to generate new forms without the need for additional ad hoc outside help.

-B: Non-Physicalism: Matter and motion alone are not sufficient to account for life; there are some systems that are irreducibly complex and require divine miracles or intelligent intervention, or both.

-A: Reductionism: Matter is everything, and everything can be fully explained in terms of accidental interactions between particles and fields. Every interaction is "accidental" because there is no sovereign Ruler of the universe, only the laws of physics themselves.