

## **New evidence for a 150 year-old conjecture regarding biological evolution**

Princeton University scientists have discovered that a fundamental protein network found in most living organisms possesses the ability to regulate its own evolution as it responds to the forces of natural selection. The work appears to offer hard evidence for an evolutionary mechanism that was first speculated to exist by Alfred Russel Wallace, the co-discoverer of the theory of evolution, in an 1858 essay. The research was published in a recent issue of *Physical Review Letters*.

The authors - Raj Chakrabarti, Herschel Rabitz, Stacey Springs and George McLendon – made the discovery while carrying out experiments on proteins constituting the electron transport chain (ETC), a biochemical network essential for metabolism. Artificial mutations in the vicinity of an ETC protein's functional active site drove its affinity for electrons in only one direction from its native value. Moreover, in proteins drawn from organisms at different stages of evolution, the electron affinity was pushed in opposite directions, implying that the affinity “bangs” from one extreme to the other during the course of evolution.

The authors sought to identify the underlying cause for this self-correcting behavior. Standard evolutionary theory offered no clues. Applying the concepts of control theory, traditionally rooted in the engineering disciplines, the researchers showed that this behavior would be possible if during the early stages of evolution, the proteins had developed a regulatory mechanism analogous to a thermostat, allowing them to fine-tune and control their subsequent evolution.

Alfred Russel Wallace had suspected that certain systems undergoing natural selection can adjust their evolutionary course in a manner “exactly like that of the centrifugal governor of the steam engine, which checks and corrects any irregularities almost before they become evident.” In Wallace's time, the steam engine was one of the only examples of a feedback controller, but examples abound in modern technology, including the thermostat and the cruise control in our automobiles. Professor Rabitz and Dr. Chakrabarti said the new research provides concrete evidence for Wallace's idea. "What we have found," Rabitz added, "is that certain kinds of biological structures exist that are able to steer the process of evolution toward improved fitness."

Evolution, the central theory of modern biology, is regarded as a gradual change in the genetic makeup of a population over time. It is a continuing process of change, forced by what Wallace and his more famous colleague, Charles Darwin, called "natural selection." In this process, species evolve because of random mutations and selection by environmental stresses. Unlike Darwin, Wallace conjectured that species themselves may develop the capacity to respond optimally to evolutionary stresses. Until the work of Chakrabarti et al., evidence for this conjecture was lacking.

The experiments, conducted in Frick Laboratory, focused on a complex of proteins located in the mitochondria, the powerhouses of the cell. A chain of proteins, forming a type of bucket brigade, ferries high-energy electrons across the mitochondrial membrane. This metabolic process creates ATP, the energy currency of life. Various researchers working over the last decade, including George McClendon and Stacey Springs at Princeton, fleshed out the workings of these proteins, finding that their electron affinities were either turned up to the maximum possible value, or down to the lowest possible value, but seldom anywhere in between. Chakrabarti and Rabitz analyzed these observations of the proteins' behavior from a mathematical standpoint, concluding that it would be statistically impossible for this self-correcting behavior to be random, and demonstrating that the observed result is precisely that predicted by the equations of control theory. By operating only at extremes, referred to in control theory as "bang-bang extremization," the proteins were exhibiting behavior consistent with a system managing itself optimally under evolution.

"In this paper, we present what is ostensibly the first quantitative experimental evidence, since Wallace's original proposal, that nature employs evolutionary control strategies to maximize the fitness of biological networks," Chakrabarti said. "Control theory offers a direct explanation for an otherwise perplexing observation and indicates that evolution is operating according to principles that every engineer knows"

Rabitz added that, "The data just jumps off the page and implies that we all have this wonderful piece of machinery inside that's responding optimally to evolutionary pressure."

The scientists do not know how the cellular machinery guiding this process may have originated, but they emphatically said it does not buttress the case for intelligent design, a controversial notion that posits the existence of a creator responsible for complexity in nature.

Chakrabarti said that one of the aims of modern evolutionary theory is to identify principles of self-organization that can accelerate the generation of complex biological structures. "Such principles are fully consistent with the principles of natural selection. Biological change is always driven by random mutation and selection, but at certain pivotal junctures in evolutionary history, such random processes can create structures capable of steering subsequent evolution toward greater sophistication and complexity."

The researchers are continuing their analysis, looking for parallel situations in other biological systems.

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