

Laws of form revisited

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Before Darwin, most biologists adhered to a platonic model of nature. This implied that the biological realm consisted of a finite set of essentially immutable natural forms that, like inorganic forms such as atoms or crystals, are an intrinsic part of the eternal order of the world. Just as, today, we account for the form of atoms and crystals by a set of physical laws or 'constructional rules', so pre-darwinian biologists sought to account for the origin of biological forms in terms of a set of generative physical laws often referred to as the 'laws of form'.

For many biologists today, platonic biology is an anachronism irretrievably laid to rest, and the idea that biological forms might be intrinsic features of nature generated by physical laws is treated with incredulity. However, recent advances in protein chemistry suggest that at least one set of biological forms — the basic protein folds —

is determined by physical laws similar to those giving rise to crystals and atoms. They give every appearance of being invariant platonic forms of precisely the type that the pre-darwinian biologists were seeking.

Protein folds, the basic constructional units of proteins, each consist of a folded chain of between 80 and 200 amino acids. Some proteins consist of a single fold, but most are a combination of two or more. During the 1970s, as the three-dimensional structure of an increasing number of folds was determined, it became apparent that the folds could be classified into a finite number of distinct structural families containing a number of closely related forms. The fact that protein folds could be classified in this manner provided the first line of evidence that the folds might be natural forms.

Further evidence that the folds do indeed represent a finite set of natural forms is provided by detailed structural studies carried out over the past two decades which have revealed that the structure of the folds can be accounted for by what amounts to a set of 'constructional rules' governing the way that the various secondary structural motifs, such as α -helices and β -sheets, can be combined and packed into compact three-dimensional structures. One is inevitably reminded of the atom-building rules governing the assembly of subatomic particles into the 92 atoms of the periodic table.

Consideration of these 'constructional laws' suggests that the total number of permissible folds is bound to be restricted to a very small number — about 4,000, according to one estimate. Confirmation that this is probably so is provided by a different type of estimate, based on the discovery rate of new folds. Using this method, Cyrus Chothia of Britain's Medical Research Council estimated that the total number of folds utilized by living organisms may not be more than 1,000. Subsequent estimates have given figures of between 500 and 1,000. Whatever the final figure, the fact that the total number of folds represents a tiny stable fraction of all possible polypeptide conformations, determined by the laws of physics, reinforces the notion that the folds, like atoms, represent a finite set of built-in natural forms.

The robustness of the folds offers another clue. The fact that the folds can retain their native conformations in the face of multiple different sorts of short-term deformations caused by the molecular turbulence of the cell, and in the face of extensive, long-term evolutionary changes in their amino-

Protein folds

"Protein folds found in nature represent a finite set of built-in, platonic forms. Protein functions are secondary adaptations of this set of primary, immutable, natural forms."

acid sequences, is precisely what would be expected if they are natural forms, specified by physical law. Again, the fact that the same fold can be specified by many different, apparently unrelated amino-acid sequences, suggesting multiple separate discoveries during the course of evolution, is further evidence that the folds are intrinsic features of the order of nature. Finally, the fact that in many cases the same fold is adapted to very different biochemical functions is precisely what would be expected if protein functions are secondary adaptations of a set of primary, immutable, natural forms.

If forms as complex as the protein folds are intrinsic features of nature, might some of the higher architecture of life also be determined by physical law? The robustness of certain cytoplasmic forms, for example the spindle apparatus and the cell form of ciliate protozoans such as *Stentor*, suggests that these forms may also represent uniquely stable and energetically favoured structures specified by physical law.

If it does turn out that a substantial amount of higher biological form is natural, then the implications will be radical and far-reaching. It will mean that physical laws must have had a far greater role in the evolution of biological form than is generally assumed. And it will mean a return to the pre-darwinian conception that underlying all the diversity of the life is a finite set of natural forms that will recur over and over again anywhere in the cosmos where there is carbon-based life. ■

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FURTHER READING

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