decreasing energy gradients and increasing channel roughness^{12,13}. Even if forest channels are somewhat wider than grassland channels, they may still act as net sediment sinks.

Despite conflicting reports of the effect of trees on channel width, there does seem to be one consistent observation — that bankside forests increase the variance in channel form. Variable channel width translates into a greater range of flow depth, velocity and substrate size, resulting in increased variability or complexity of habitats; all of these are features that in my experience serve as a mantra for stream ecologists. Hence, evaluation of geomorphological and ecological impacts may yield contradictory conclusions; in some cases a little extra erosion may provide a more varied, diverse and productive habitat.

Trimble's paper⁴ illustrates the frustrating complexity facing those charged with managing, restoring and protecting the world's river systems. Single-recipe approaches provide a poor foundation for management of rivers and streams, in part because they often ignore connections between physical and biological processes. Moreover, coupling predictions of channel response to stream ecology and public-policy considerations further complicates an inherently challenging problem.

That leaves us with two distinct choices for ecologically orientated river management: either trust that 'natural is best' and promote restoration of riparian forests, or treat each river on a case-by-case basis. Trimble's cautionary thoughts on forest restoration would suggest the latter course of action. Unfortunately, few of those who work in this area receive the advanced training necessary to adequately understand and diagnose channel conditions. So, for now, perhaps it is wiser to favour nature's course. Continued research is needed into general models of channel response, and into the integration of fluvial geomorphology into river-system restoration and management. But the greater need is the establishment of a corps of river professionals whose expertise spans geomorphology, ecology and public policy. □

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Protein folding

The difference with prokaryotes

Mary-Jane Gething

When proteins are made, they start off as chains of polypeptides. The study of how they come to fold into their correct three-dimensional structure is a wonderfully complicated business that has been tackled in numerous ways. In their paper on page 343 of this issue¹, Netzer and Hartl explore a somewhat neglected approach — that of looking at differences in the folding pattern of nascent polypeptides in the cytoplasm of prokaryotic and eukaryotic cells. In doing so, they tell us a great deal about some basic issues to do with protein folding, but we need to step back a little to understand why.

Anfinsen's classic *in vitro* experiments on the refolding of ribonuclease^{2,3} demonstrated that all of the information required to determine the final conformation of a protein can reside in the polypeptide chain itself: given the appropriate conditions, a denatured enzyme can refold into its native conformation in the absence of any other protein. Anfinsen's work was of seminal importance in establishing the central principle of self-assembly of proteins, but it probably delayed by a decade or two the initiation of investigations of protein folding *in vivo* — the trouble was we believed that the polypeptide sequence was all that there was to it. Nevertheless, over time we came to recognize that efficient folding *in vitro* is frequently limited to small, single-domain proteins and usually occurs under conditions of protein concentration, temperature, ionic strength and pH far removed from those occurring within cells.

The search for agents that support the folding of polypeptides under physiological conditions led to the characterization of a wide variety of molecular chaperones and folding catalysts that preside at the birth, maturation and death of most, if not all, proteins within cells^{4,5}. These chaperones and folding catalysts do not determine the final conformation of the polypeptide substrate (Anfinsen rules OK!); rather, they increase the efficiency of folding by inhibiting off-pathway aggregation reactions or catalyse rate-limiting isomerization steps. They are members of large protein families, and are present in all cell types, from prokaryotes to humans, and in all compartments of eukaryotic cells. The high degree of conservation of the members of each family during evolution has lulled us into believing that the process of protein folding is likely to be mechanistically similar in different organisms. This is where the new work of Netzer and Hartl¹ comes in.

The original premise underlying their study was that evolution of eukaryotic proteins by gene fusion or exon shuffling demands that the newly combined domains

must be able to fold independently of one another. Although this idea seems perfectly intuitive (at least in retrospect), to my knowledge its implications with respect to protein-folding mechanisms have not previously been tested. The study reveals that protein domains (which usually range from 100 to 300 amino acids in length) can indeed fold sequentially and independently when synthesized from a eukaryotic ribosome. In prokaryotes, however, folding of individual domains is delayed until the complete polypeptide chain has been synthesized. This latter situation can result in inappropriate interdomain interactions or aggregation — which are indeed often observed when complex eukaryotic proteins are synthesized in the prokaryote *Escherichia coli*.

Comparison of the protein-size profiles of different prokaryotic and eukaryotic organisms, made possible by the completion (or near completion) of sequence analyses of their genomes, reveals that prokaryotes may cope with this difficulty, at least in part, by restricting protein size and thus the complexity of protein-domain organization (see Fig. 1 of Netzer and Hartl's paper, page 343). Nevertheless, a lot of proteins in *E. coli* are more than 300 residues in length; many of them probably correspond to multifunctional proteins that have arisen by fusion of genes encoding the individual enzymatic activities or functions⁶. Given a post-translational mode of folding, such fusions would presumably have been productive only in cases where the individual domains could fold independently. In eukaryotes, however, the rapid evolution of multidomain proteins by gene fusion or exon shuffling (made possible following the development of complex genes) would not be restricted by any requirement that the component domains should not interfere with one another during the folding process.

Netzer and Hartl's work¹ also does much to resolve, intellectually if not mechanistically, a previously open question — why efficient protein folding in prokaryotes seems to rely so heavily and generally on the chaperonin GroEL, the eubacterial member of the Cpn60 (also known as Hsp60) family^{5,7}, whereas in the eukaryotic cytosol the chaperonin homologues (known as CCT^{7,8} or TRiC⁵) appear to play a much more limited role. GroEL and its co-chaperonin GroES form a cylindrical complex that encloses a central cavity in which polypeptides can fold sequestered from the cellular environment⁵. The observation that most polypeptides synthesized in *E. coli* can associate with GroEL prior to folding (F. U. Hartl, unpublished observations) may reflect the fact that they

must fold post-translationally. CCT chaperonins apparently interact with very few substrates, including actin and tubulin⁹. Netzer and Hartl point out that, although actin is a multidomain protein, its domains are composed of discontinuous amino-acid sequences, and therefore it would not be expected to fold co-translationally. So CCT chaperonins may have been retained in eukaryotes for the specific but limited task of coping with polypeptides that cannot fold in a stepwise fashion, domain by domain, as translation proceeds.

The molecular mechanisms underlying the different treatment of nascent polypeptides, following synthesis by prokaryotic and eukaryotic ribosomes, remain to be defined. Netzer and Hartl rule out the higher speed of translation in bacteria as a significant factor, but raise the possibilities that the prevention of folding of ribosome-bound polypeptides in *E. coli* might be effected either by ribosomal components or by molecular chaperones. One *E. coli* chaperone that can be exonerated is GroEL itself, because it does not recognize ribosome-bound chains⁵. By con-

trast, Hsp70 chaperones^{5,10} do interact with ribosome-associated nascent polypeptide chains, both in *E. coli* and in mammalian cells. Whether a previously unsuspected difference in the way in which prokaryotic and eukaryotic Hsp70 proteins interact with newly synthesized polypeptides underlies the failure of prokaryotes to support co-translational folding, or whether other translational co-factors are involved, is sure to be the subject of intensive studies in the coming months. □

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Extraterrestrial impacts

Earth rocked by combination punch

Dieter Stöffler and Philippe Claeys

The 100-km-diameter Popigai structure in Siberia is probably the fifth largest impact crater on Earth. Its age has been disputed — it could be anything from 5 to 65 million years (Myr) old. But this controversy appears to be finally settled: on page 365 of this issue¹, Bottomley *et al.* report ages of 35.7 ± 0.2 Myr for rocks from the Popigai crater that were melted by the impact. That means that 35.5 million years ago, in the space of only a few hundred thousand years — or perhaps much less — two large asteroids or comets struck the Earth, one in Siberia and another just off the west coast of North America.

The Late Eocene age for Popigai opens up intriguing questions about how two large impacts in quick succession might have affected the Earth. The period from the Late Eocene to the Eocene/Oligocene boundary (which is dated at 33.7 ± 0.5 Myr ago) is marked by the most severe mass extinction since the dinosaurs disappeared 65 Myr ago. The climate also worsened considerably in the Late Eocene, with cooling oceans and the first appearance of ice sheets in Antarctica.

Could these changes be the result of two almost coeval large impact events? We now know¹ that the Popigai crater is the same age as impact indicators (iridium and shocked quartz) found below the Eocene/Oligocene boundary in the Massignano section, Italy^{2–4}, which are dated radiometrically using volcanic ash layers at 35.7 ± 0.4 Myr

old^{2,3}. However, compositional evidence linking the Popigai crater and the Massignano ejecta is lacking; more work on this topic is urgently required. But the age coincidence is remarkable.

Excitement about the Popigai date grows in the light of the discovery a few years ago of a contemporaneous impact event on the other side of the world: the 85-km-diameter Chesapeake Bay impact structure, off the Virginia shore^{5,6}. The Chesapeake Bay crater had already been dated at 35.5 to 35.2 Myr old⁶. It is probably the source of the huge field of tektites (characteristic glassy nodules produced by melting of the target rock in an impact event) strewn mainly over Georgia, as indicated by the chemical similarities between the glass and the Chesapeake Bay target rocks^{7,8}. Similarly, the crater appears to be the source of microtektites and layers of excess iridium found on Barbados and in several ocean-floor drilling cores (such as DSDP 612), and dated at 35.4 ± 0.6 and 35.5 ± 0.3 Myr old^{9,10}, respectively.

So, within the error bars, the Popigai and Chesapeake Bay craters are the same age; at most, they occurred a few hundred thousand years apart. The tremendous energy released by these two successive huge impacts may have induced the long-lasting perturbation of the global environment which led to the terminal Eocene cataclysm and global changes.

We finally have a second solidly based case study, after the Cretaceous/Tertiary

100 YEARS AGO

We endeavoured before to ascertain what density of atmosphere might be conceded to the moon. This density being very feeble, it follows that the surface of our satellite must now be at a low temperature — at least, near the poles. There is even cause to ask if it is not totally or partially covered with ice. The most complete representation of the southern region ... inclines us to the opposite view — that is to say, that the presence of a great accumulation of ice must be considered improbable, as well for the polar caps as for the equatorial region. One is, therefore, led to imagine that the total moisture on the surface must have disappeared, undoubtedly by penetration into the interior of the globe, before the polar regions sank permanently beneath freezing-point. ... The cooling of our satellite, more rapidly than that of the earth, has shortened the period of condensation of the vapours. The water was filtered as fast as it was formed in innumerable volcanic orifices, which seemed prepared to receive it. Pl. vi. gives us an idea of the abundance of these openings in the neighbourhood of the pole, and one is led to think that the same constitution must have existed on the whole of the moon previously to the formation of seas.

From *Nature* 22 July 1897.

50 YEARS AGO

[Dr. Fosdick] does not deny that knowledge is dangerous, but he insists that the answer does not lie in trying to curb science or to fix boundaries beyond which intellectual adventure should not be allowed to go. The search for truth, he maintains, is, as it always has been, the noblest expression of the human spirit. Man's hunger for knowledge about himself, his environment and the forces by which he is surrounded, gives human life its meaning and purpose, and clothes it with final dignity. Civilisation is not being betrayed by science: the danger lies in the failure to use science wisely. ... The fundamental issue of our time is whether we can develop understanding and wisdom reliable enough to serve as a chart in working out the problems of human relations, or whether our lopsided progress will be allowed to develop to a point that capsizes our civilization in a catastrophe of immeasurable proportions. From *Nature* 26 July 1947.