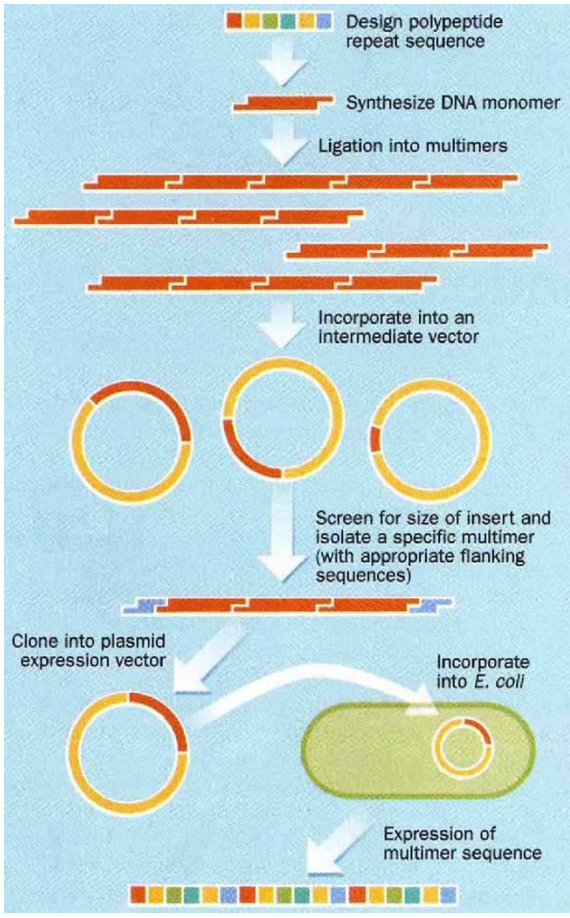
self-replicating circular strand of bacterial DNA) from *Escherichia coli*. The target polymer is then expressed *in vivo* and, if necessary, cleaved from its flanking sequences.

Tirrell's studies have so far focused primarily on two classes of polypeptide: sequences based on repeats of glycine–alanine, and glutamic acid polymers. One question that he has been able to address concerns the formation of polymer liquid crystal phases. Poly(benzyl glutamate) (PBG) is known to form at least one nematic phase, in which the chains exhibit orientational but not positional order. Small-molecule nematic liquid crystals often undergo a transition to a smectic phase as temperature is lowered, in which the molecules are arrayed in layers with a regular repeat distance perpendicular to the layers. But the polydispersity in chain length of regular PBG may be expected to inhibit the formation of a smectic phase.

To address the issue of whether monodisperse PBG can form a smectic phase, Tirrell prepared poly(glutamic acid) via his microbial factories and then used standard synthetic methods to derivatize the chains to PBG. The resulting compound does indeed show a texture, under the polarizing microscope, that is suggestive of a smectic phase. But confirmation of this identification must await diffraction studies.

Incorporating more complex amino-acid sequences into these artificial polypeptides should allow the exploration of protein tertiary structure using model systems, and the design of polymer crystal structures using structural motifs familiar in proteins. Tirrell's group has built polymers containing glycine–alanine repeat segments (GlyAla) interrupted at every third step by glycine–glutamic acid units (GlyGlu). Strings of (GlyAla) are known to form β-sheets, while the hope was that the (GlyGlu) sections would serve to introduce turns, allowing the sheets to stack in smectic-like arrays. X-ray studies confirm that the polymer adopts the expected folded-β-sheet structure.



Producing polymer molecules to order.

Chemically modified amino-acid residues might afford still more exotic materials. Tirrell described an example which might be dubbed a 'non-stick protein', containing fluorinated amino-acid residues. The idea was that the hydrophobic fluorine-containing groups might segregate from the interior to the surface of the folded polymer, engendering unusual surface properties.

The polymer is of the form $[(\text{Ala–Gly})_3\text{–F-Phe–Gly}]_x$, where F-Phe is a fluorinated form of phenylalanine. Once the artificial gene is incorporated into the bacterial cells, a strain must be developed that cannot make unfluorinated phenylalanine and can use the derivatized form in protein synthesis. Tirrell and colleagues found good expression of the fluorinated polypeptide, with almost complete substitution of phenylalanine by the fluorinated variant. The material is rather insoluble in water, as one might expect; but its three-dimensional structure, and in particular the question of where the fluorine sits, remains to be resolved.

Particularly enticing from the perspective of materials design is the possibility of modifying structural proteins such as silk and collagen to improve their mechanical and chemical properties. Silk has long been hailed as a spectacular example of the superior properties of biomaterials; but the opportunity to improve on nature is always hard to resist. □

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DAEDALUS

Dream no more

THE problem of free will, and the origin of mental inspiration, have long bothered philosophers. In the 1930s, it was suggested that the brain might amplify quantum uncertainty up to macroscopic levels. More recently a mechanism has been proposed: the firing of neurons by radiation. High-energy events in the brain, perhaps generating small bursts of neurotransmitter by some radiolysis reaction, fire neurons at random. Every so often, this 'noise' happens to trigger some critical neuron, one whose output avalanches into a whole new train of thought. This is the magical process of sudden whim or inspiration. External radiation is well blocked by the skull; most such events must come from decay of the brain's internal content of ^{14}C and ^{40}K. So Daedalus plans to remove these isotopes from the brains of volunteers, and observe the changes.

It will be a long job. Plants must be grown with ^{14}C-free CO_2 (from burning fossil fuel) as their sole carbon source. Their fertilizer must be depleted in ^{40}K by standard isotope separation methods. When harvested, they will form a rigorously radiation-free vegetarian diet. Volunteers fed exclusively on this diet will, by the steady metabolic turnover of all their tissues, slowly come to be radiation free themselves.

Deprived of inspiration, but with their memory and reasoning power still intact, Daedalus's volunteers will inhabit a very ordered mental world. Calmly logical in a crisis, they will be highly predictable in routine conditions. A radiation-free diet may help hyperactive children and butterfly-mind geniuses to complete the tasks they begin. In psychiatry it may quench the insane whims of psychotics and the chaotic enterprise of manics: but obsessives, of course, would become more obsessive than ever. The diet might even replace gaol for impulsive criminals. Deprived of random temptation, they might abandon crime: if not, they would be predictable enough to catch easily. On giving up the diet, a user would slowly take up natural levels of radioisotopes and, over several months, recover his previous personality.

An isotope-enriched diet should have the converse effect. Scientists whose inspiration has failed them and novelists paralysed by writer's block might be revitalised by a diet carefully elevated in ^{14}C and ^{40}K. Daedalus wonders if the physicists of the heroic age owed their towering creativity to the radioactivity they studied so carelessly. If so, modern physicists yawning over yet another plodding, uninspired theory or experiment can blame today's safety regulations.

David Jones