HYDROGELS

Wet or let die

Proteins are like fish in that they need water to survive — without it they lose vitality and become unable to carry out their functions. A new hydrogel material for protein microarray chips keeps the proteins wet and lively.

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High-density DNA microarray chips have been enormously useful tools for probing deep and wide-ranging questions in biology, but they can't track protein activities. Although DNA chips can be fabricated and stored dry for long periods of time, the formation of high-density protein chips to fully understand protein functions has so far been a tremendous challenge. This is because proteins need to be in a wet environment in order to remain structurally intact and carry out their biological functions. Despite the serious effort and progress made in fabrication techniques, this simple requirement is still a barrier to the development and use of suitable protein chips. In this issue of *Nature Materials*, Itaru Hamachi and his group present a new hydrogel scaffold designed to overcome this barrier[1].

Complex cellular functions are carried out largely through the intricate and subtle interactions of proteins — protein–protein, protein–RNA, protein–DNA, and protein–cofactor (a small molecule essential for some proteins to carry out their function). In the theatre that is the biological cell, proteins are the main actors, and DNA is the script. A clear and quantitative view of how many actor proteins are on the stage at any given moment is crucial for understanding cellular function. Protein chips can provide us with that view.

The main interest of Hamachi's group has been in synthesizing and screening new biomaterials from combinatorial and composite libraries of sugars coupled with other small molecules. Their effort has indeed paid off in this important discovery. Their new biomaterial is a hydrogel formed through the supramolecular assembly in water of a small molecule (less than 700 daltons) with a hybrid structure. At one end, this molecule contains a polar moiety (a sugar) that interacts favourably with water — that is, it is hydrophilic — and at the other end, linked through an amino acetate unit, are two non-polar moieties (two methylcyclohexyl rings), forming a hydrophobic group.

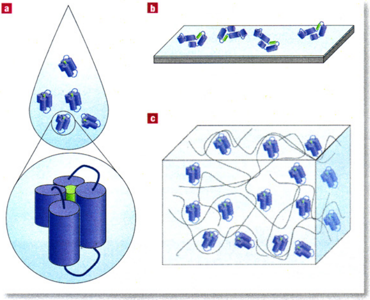

Figure 1 The correct environment for proteins. a, When proteins are in an aqueous solution, they can fold properly, with their hydrophobic core (the green cylinder) tucked up inside and their hydrophilic shell (the blue cylinders) exposed. **b,** When proteins are left to dry or if they encounter a hydrophobic surface or solvent, they lose their folded structure and turn themselves inside out. **c,** When proteins are embedded in a hydrogel scaffold made of nanofibres, such as the one synthesized by Hamachi and colleagues[1], the environment that surrounds them is nearly 99% water. They can fold properly and thus carry out their full biological functions.

This material has an extremely high affinity towards water molecules, and thus the ability to form a hydrogel at very low concentrations (in the range of 0.1% or 1 mg per ml), creating a dense network of nanofibres. Within this network, water molecules can easily penetrate and dwell in the hydrophilic cavities (see Fig. 1), which creates a habitable environment where proteins can carry out their normal functions, such as catalysis, for instance. This is a significant step forward from current protein