T he recent explosion of research in nanotechnology, combined with important discoveries in molecular biology, have created a new interest in biomolecular machines and robots. In this issue of Nature Materials, Knoblauch et al. show that a natural assembly of proteins—extracted from a legume plant and placed in an artificial environment—can contract and expand in two orthogonal directions1. This primitive biological muscle, baptized ‘forisome’ by Knoblauch and colleagues, exerts relatively large forces in response to small changes in the concentration of calcium ions and could be used as a novel micromotor.

The main goal in the field of biomolecular machines is to use various biological elements—whose function at the cellular level creates a motion, force or a signal—as machine components that perform the same function in response to the same biological stimuli but in an artificial setting. In this way, proteins and DNA could act as motors, mechanical joints, transmission elements or sensors. If all these different components were assembled together they could potentially form nanodevices with multiple degrees of freedom, able to apply forces and manipulate objects in the nanoscale world, and even travel in a nanoscale environment.

All this might sound like science fiction, but scientists have already started working to make it a reality. Several biomolecular components have been proposed as motors, switches and sensors. A recent report2 shows how nanodevices can be powered by ATPase. This motor protein, strikingly similar in structure to the rotary motors in our daily appliances, is normally involved in producing energy for the cell1. Its function is therefore dependent on ATP, a molecule with high chemical energy. In general, the presence of ATP is a requirement for the majority of motor-like biomolecules, such as kinesin1, myosin4 and dynein4. This constitutes a practical limitation as it means that these motors need a very specific chemical environment to function, which might be difficult to recreate in real-world applications1. Knoblauch and colleagues’ findings show us a different way to go, an ATP-independent motor whose function is less bound to strict chemical requirements. Several other non-ATP-based motors have been proposed, such as DNA-based nanoactuators8, flagella motors9 and viral protein linear motors10. But whereas all these have dimensions of the order of several tens of nanometres, Knoblauch’s forisomes are macroscopic assemblies whose size is in the order of micrometres. So, although they could not be used to develop devices at the nanoscale, they are easy to manipulate using current state-of-technology tools and their ‘technological readiness’ is therefore higher than that of other non-ATP-based motors.

The macroscopic protein assembly of forisomes is part of a safety mechanism inside legumes. The transport of water and other minerals within different parts of the plant takes place through tubular structures called sieve elements, from which the forisomes are extracted. When a rupture occurs, due to mechanical damage for instance, the flow through the sieve elements is interrupted by the formation of plugs in the tubes. This stopcock-like effect is attributed to the reversible swelling and contraction of the proteins in response to changes in the concentration of Ca2+ ions. In the presence of Ca2+, the forisomes assume an ordered state whereas in the absence of Ca2+ ions (left) the forisome is in its narrow extended state and after cycling the Ca2+ ion concentration result in a periodic, reversible motion of the payload.

**Figure 1** A potential device using a forisome as a mechanical element. A biomolecule, such as a protein, attached to the moving forisome is being pushed up and pulled down as a payload. The forisome and the payload are confined to operate in a cylindrical region. In the absence of Ca2+ ions (left) the forisome is in its narrow extended state whereas in the presence of Ca2+ ions (right) it contracts in length and expands in diameter. Cycling the Ca2+ ion concentration result in a periodic, reversible motion of the payload.
A vision of biomolecular machines in the nanoworld. Ultra-nature robotic systems and nanomechanical devices may become the hardware of future manufacturing, medical, military and space operations. These devices will be lightweight and hence easy for launching in remote worlds or introduced into environments difficult to reach. The advantage of using nature’s machine components is that they are highly specific, well optimized and their performance is excellent. For example, this figure shows a hypothetical model of a biomolecular nanorobot—a carbon nanotube with peptide limbs attached to the surface and a propeller molecule at the end. The nanorobot flows through the vessel, finds an infected cell, attaches to it and projects a drug to repair or destroy it.

(swollen) conformation that blocks the fluid flow, whereas in the absence of Ca²⁺, they take on a disordered (extended) shape that leaves the sieve elements unobstructed. Hence nature has provided us with a ready-made structure that changes conformation from a narrow cylindrical structure to a swollen balloon-like shape and allows the application of force in two orthogonal directions (Fig. 1). The authors reproduce this behaviour in the laboratory by attaching individual forisomes to a glass pipette tip and monitoring the conformational change in response to changes in calcium ion concentration and pH. Their experiments provide answers to the most immediate question: what drives the forisomes, how fast is the response and will they endure repeated contractile cycles without failing?

The experiments performed reveal some very important performance characteristics of the forisomes. The longitudinal contraction is of the order of 30%, whereas the diameter expansion is of the order of 120%. This strongly anisotropic behaviour might be useful in future mechanical applications in which short displacements in one direction could be associated with very large displacements in the other. Simple force measurements show that forisomes are able to apply forces of 0.1 µN, which are substantial considering their size. Changes in the concentration of calcium ions or pH variations in a certain range produce fully reversible motion of the forisomes. Reversibility is a very important property for protein motors, and usually a difficult one to ascertain. It means that the same motor can effect a movement in a direction and then return to its original position without the need for an antagonistic motor. Another remarkable feature of forisomes is their fast response to pH changes, which allows the motor to be driven by automated pH control, and eventually could lead to the development of fully autonomous, computer-controlled, forisome-powered devices.

The future of bionano machines is bright (see Fig. 2). We are at the dawn of a new era in which many disciplines will merge including robotics, mechanical, chemical and biomedical engineering, chemistry, biology, physics and mathematics so that fully functional systems will be developed. However, there are many hurdles still to be overcome to reach this goal. The development of a complete set of different biomolecular components and the ability to interface or assemble them, are some of the challenges to be faced in the near future. The problems involved in controlling and coordinating several biomolecular machines will come next.

References