BIOMOLECULAR ACTUATORS

Muscle on demand

Light-activated protein actuators composed of bioengineered motors and molecular scaffolds achieve millimetre scale mechanical work, which holds promise for microrobotics applications.

Henry Hess

In cells, contractile structures (e.g. stress fibers[1]) dynamically assemble when needed from cytoskeletal filaments and motor proteins to generate forces that aid cell attachment and migration. These biomolecular structures lack the precise molecular organization of muscles, which are superbly adapted to directed force generation, but can assemble when and where they are needed mainly to generate static contractile forces. Now writing in Nature Materials, Nitta and colleagues report an engineered system where the formation of a contractile structure takes place on demand in a solution of cytoskeletal filaments and motor proteins[2]. The contractile gels with millimeter scale dimensions can form precise shapes when stimulated with patterned light and achieve microNewton forces that can operate, for example, miniature pliers (**Fig. 1**).

The construction of active, contractile materials resembling muscles has been a long-standing goal in materials science. Early milestones were carbon nanotube actuators[3] and artificial muscles from sewing line and fishing thread[4]. However, mimicking muscle more closely by relying on molecular motors to power contraction has only recently been demonstrated using light-driven synthetic molecular motors[5]. Nitta and coworkers approach the challenge from a different angle, relying on biomolecular motors produced with biotechnological methods, to achieve contraction on the millimeter scale powered by chemical energy in the form of ATP. The key idea is to capitalize on prior knowledge about the active self-assembly of cytoskeletal filaments and motor proteins[6] to construct molecular building blocks capable of organizing themselves into larger scale contractile structures. Inspired by the structure of muscle, the authors developed an active biomolecular system entailing engineered filamentous scaffolds made from the fusion of calmodulin, a calcium ions binding protein, with light meromyosin, the tail portion of myosin, and microtubule-associated motor proteins resulting from the fusion of kinesin-1 with a calmodulin binding sequence. Upon the photo-induced release of calcium ions, the kinesin-1 motors bind to the filamentous scaffold, creating bipolar filaments that resemble myosin (“thick”) filaments in muscle. Contraction of the emerging network of kinesin-carrying filaments and microtubules is achieved by microtubule sliding due to the action of the kinesin motors in the presence of ATP. Since the sequential assembly and contraction processes are initiated by the light-induced release of calcium ions, the contractile activity can be controlled both in time and space via patterned illumination.

The work by Nitta and colleagues is highly multiscale, from the design and construction of the molecular components using molecular biology techniques, over the self-assembly of the molecular components into nanoscale structural elements (microtubules and kinesin filaments) and the subsequent non-equilibrium self-organization of these nanoscale elements into interacting microscale subunits, to the formation of the contractile millimeter scale structure from these subunits. It also highlights the potential of a biotechnological approach[7], and the results can now be compared with the chemistry-based approach of employing synthetic molecular motors. Silicon-based nanofabrication of motors is the third contender[8], integrating well with the solar economy but less well with biomedical applications in drug delivery and microsurgery.

The approach, of course, has still unresolved problems, as the authors point out. Repeated cycles of contraction and relaxation would require the removal of calcium ions, something muscles achieve with a dedicated pumping mechanism. The mechanical stresses generated (0.2 kPa) are a thousand-fold lower than those generated by muscle and ten-fold lower than those generated by stress fibres but compare favourably to those generated by actuators based on synthetic molecular motors.

From a higher vantage point, it is interesting to consider the need for contractile materials. While actuation in animals is typically achieved via the generation of tensile forces by contracting muscles, modern technology typically mimics plant biology[9] in relying on extensile forces generated by pneumatic and hydraulic systems. These systems in turn are powered by motors. Miniaturization presents a challenge to this dichotomous design, since frictional losses increase and motor efficiencies drop as the systems sizes shrink. To continue on the technological path towards smaller and more numerous actuators[10] an integration of hydraulics and motor at the nanoscale is desirable (**Fig. 2**).

Nanoscale integration is achieved in the sarcomere, the basic functional unit of the muscle, where the force generation by myosin motor proteins leads to the interdigitation of thick and thin filaments without the generation of fluid flow. An almost crystalline stacking of sarcomeres into muscle tissue then scales force and velocity up, providing actuators suited for mosquitoes and whales. Actuators for future ubiquitous microdevices will similarly require molecular motors, or a mechanism used to generate mechanical work from some energy input. Similar to the first steam engines, the motor's energy conversion efficiency has to exceed 1%, otherwise the actuators relying on it would consume an unacceptably large portion of the energy budget[10]. This efficiency has to be maintained as the motors are integrated into a system which achieves force multiplication, and a method for controlled activation has to be implemented. The final challenge is to maintain the assembly in an operational state for an extended time. The work by Nitta and coworkers is the most fully developed effort to date to meet these challenges on the biotechnological route. As in the early days of climbing Mt. Everest, the most feasible approach to the peak of potential performance is still under consideration.

Competing Interest

The author declares no competing interests.

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Figures legend

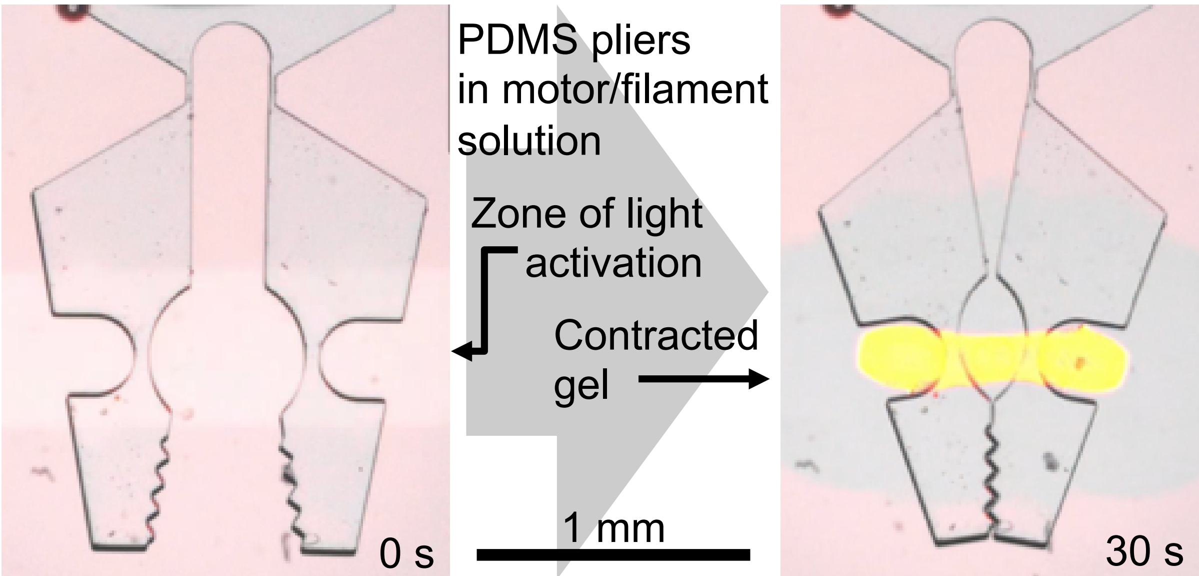
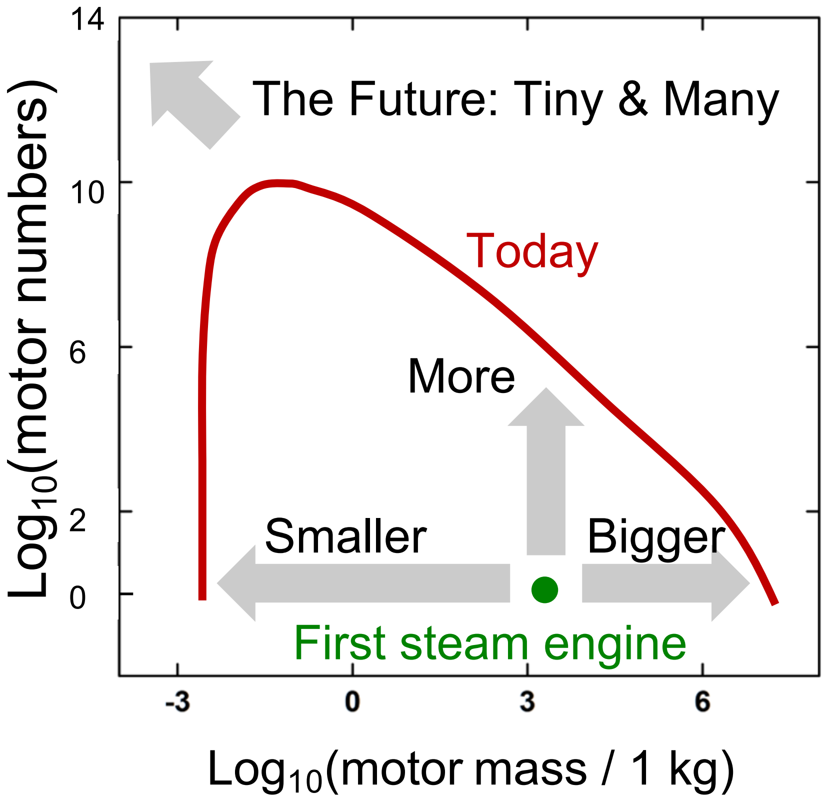


Figure 1. Pliers closing with active protein networks. Light-induced release of caged calcium ions leads to the localized assembly of a network of kinesin motor protein-carrying filaments and microtubules, which is followed by motors sliding on microtubules to contract the entire network. The millimeter scale network generates microNewton forces that are sufficient to actuate the polymeric pliers. Figure adapted with permission from ref. 2, Springer Nature Ltd.



åFigure 2. Motor abundance varies inversely with size and increased as technology progresses. Since the first steam engine has been invented, engines, motors and actuators have multiplied and evolved into serving an immense variety of functions. Today, the earth is occupied by tens of billions of small electric motors spinning hard drives, several billion motors powering appliances, a billion car engines, hundred million truck engines, and so on, all the way to a few giant turbines for pumped-storage hydroelectric power stations weighing hundreds of tons. While the biggest engines attract the attention, the growth is on the small side where continuously shrinking motors aim to become as ubiquitous as mosquitoes.