finding *in vivo* using neurons taken from patients with C9-ALS. HRE expression disrupted the nuclear import of fluorescent test substrates and of normal nuclear proteins — most notably TDP-43, which forms misfolded aggregates in the degenerating motor neurons of most people with ALS. Freibaum and colleagues observed nuclear-membrane irregularities in HRE-expressing cells and demonstrated that G_4C_2 HREs inhibit nuclear RNA export, an effect that was relieved by reducing the expression of genes that suppressed G_4C_2-mediated toxicity. Together, these findings established a strong connection between defective nuclear trafficking and neurodegeneration (Fig. 1).

Do DPRs contribute to G_4C_2 toxicity? Both studies detected G_4C_2-derived DPRs, but neither could show whether these DPRs contributed significantly to toxicity. In the third study discussed here, Jovičić *et al.*[3] addressed this point directly, performing a genetic screen to identify genes that lessened or worsened the toxicity caused by a PR_{50} DPR in the yeast *Saccharomyces cerevisiae*. Because PR_{50} was expressed from synthetic DNA and not from a G_4C_2 HRE, toxicity should derive from the DPR itself, rather than from its parent RNA. Six of the strongest suppressors of PR_{50}-associated toxicity in the researchers' screen encoded members of the karyopherin family of nuclear-import proteins. The screen also suggested that the genesis of ribosomes (the cellular machinery that produces proteins) goes awry in PR_{50}-expressing yeast. In the future, even more leads are likely to be mined from these genetic data.

These three studies take us to a higher plane of understanding of *C9ORF72*-associated ALS, with a focus placed squarely on the nuclear pore. For the future, the newly identified toxicity-suppressing genes will need to be tested in mammalian models of G_4C_2 expansion and DPR toxicity, probably using recently developed mouse strains[19]. The findings also raise the question of whether nuclear-trafficking defects contribute to neurotoxicity in other types of ALS. Neurons have a limited ability to replace damaged nuclear-pore complexes, and age-dependent decreases in nuclear integrity have been postulated as a risk factor for ageing-related disease[20]. Thus, enhancers of nuclear import should be tested in other ALS models, particularly those in which TDP-43 aggregation is observed.

The genetic studies have not resolved whether one mechanism of toxicity predominates in C9-ALS. At face value, the data suggest that G_4C_2-containing RNAs and G_4C_2-derived DPRs elicit toxicity through an overlapping set of nuclear-pore proteins. However, it remains possible that DPRs contribute to neurotoxicity directly in flies. This question could be answered by investigating whether the nuclear-import enhancers picked up in the G_4C_2 screens can rescue neurodegeneration in flies expressing toxic DPRs. It will also be important to further characterize G_4C_2–RanGAP interactions, and to determine whether DPRs bind nuclear-pore proteins. Finally, because both DPRs and G_4C_2 HREs reportedly disrupt a subnuclear structure called the nucleolus[10,13], the relationship between this mechanism and nuclear-membrane defects should be deciphered.

Can our understanding of toxic G_4C_2 RNA be leveraged for therapy? Zhang *et al.* reversed the rough-eye trait by feeding $(G_4C_2)_{30}$ flies either a compound that disrupts G_4C_2–RanGAP binding or a small-molecule inhibitor of nuclear export. The three studies also identified other genes that may be 'druggable', including those encoding proteins that oppose RanGAP. Development and preclinical testing of modulators of nuclear import or export is certainly warranted. No doubt, genetic studies such as the three discussed here will identify other nodes of therapeutic interest. ■

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SOFT MATTER

Frictionless fluids from bacterial teamwork

By increasing the sensitivity of an established technique, researchers have shown that swimming bacteria can make frictionless fluids — with potential applications in areas such as microfluidics.

M. CRISTINA MARCHETTI

The viscosity of a liquid is a measure of its resistance to flow. In general, denser fluids are more viscous and require more energy to get them to flow through a pipe. Flow with no energy dissipation is a hallmark of exotic states of matter such as superfluidity and superconductivity. Key to these exotic states are quantum effects that dominate at ultralow temperatures — turning liquid helium, for example, into a superfluid that flows without friction through cracks as thin as molecules. Writing in *Physical Review Letters*, López *et al.*[1] demonstrate that *Escherichia coli* bacteria swimming in a fluid can organize themselves to counterbalance the energy loss resulting from viscous dissipation and thereby dramatically lower the fluid's viscosity, driving it to vanish or even to become negative.

In 2004, it was predicted[2] that unicellular swimming organisms could substantially change the viscosity of a fluid on the basis of a hydrodynamic theory[3] of active fluids (liquids consisting of self-propelled particles). This suggestion was confirmed by numerical solutions[4,5] of the theory, which revealed the possibility of vanishing viscosity for suspensions of motile bacteria. Pioneering experiments subsequently confirmed a reduction of viscosity in suspensions of the bacteria *Bacillus subtilis*[6] and *E. coli*[7]. A concurrent study[8] demonstrated the sensitivity of this effect to the microscopic cellular-propulsion mechanism by revealing an increase in viscosity for dilute concentrations of the alga *Chlamydomonas reinhardtii*; however, this behaviour remains puzzling.

Detailed calculations[9–12] of the response of dilute suspensions of swimmers to an externally imposed shear flow (which induces the velocity profile shown in Fig. 1a) have provided quantitative expressions for viscosity changes for small volume fractions of bacteria. Demonstrating that a bacterial suspension can

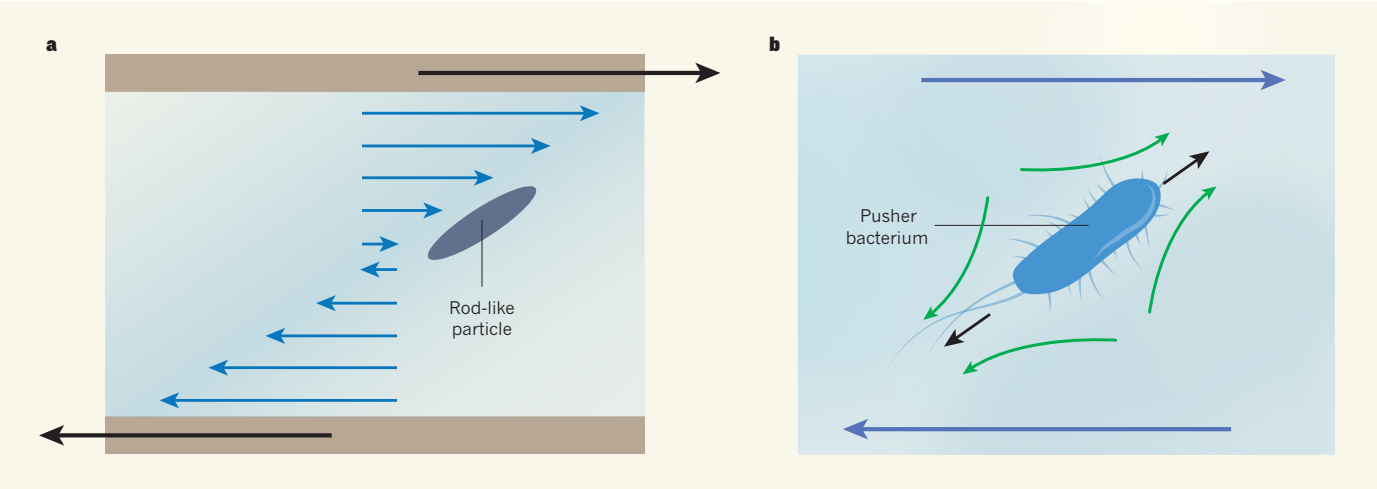

Figure 1 | Viscosity modulation by rod-like bacteria. **a**, Shear flow (blue arrows) can be imposed on a fluid between two plates by applying equal and opposite forces (black arrows) on the plates. Rod-like particles suspended in the liquid respond by orienting their long axes along the direction in which the flow tends to 'stretch' the fluid. **b**, Bacteria such as *Escherichia coli* are 'pusher' swimmers, which use their rear flagella appendages for propulsion. Pushers exert equal and opposite forces (black arrows) at their front and tail. In an external shear flow (blue arrows), they orient along the stretching direction of the flow and generate flow fields (green arrows) that further push the fluid in the same direction as the shear flow, reducing the fluid's viscosity. López *et al.*[1] report that suspensions of *E. coli* can generate fluids with zero, or even negative, viscosity.

achieve a state of vanishing, or even negative, viscosity was previously impossible, however, because this requires measurements of tiny shear stresses.

López and colleagues overcame this problem by adapting an old-fashioned rheometer — a device used to measure fluid viscosity. A simple rheometer consists of inner and outer cylinders that can rotate relative to each other. A fluid is placed in the annulus between the cylinders and one of the cylinders is rotated at a set rate, shearing the fluid. The liquid drags the other cylinder, exerting a torque on it. From measurements of this torque, one can infer the shear stress and thus the fluid viscosity, defined as the ratio of stress to the applied shear rate.

The authors modified this device by controlling the rotation of the inner cylinder using a computerized feedback mechanism. This set-up maintains zero torque, allowing highly sensitive measurements of ultralow shear stresses. The researchers also suspended bacteria in a medium that allows the microbes to remain motile but not to divide, enabling control of the bacterial concentration.

Importantly, López *et al.* were able to demonstrate the existence of states of arbitrarily small viscosity, in a regime in which the viscosity did not depend on the imposed shear rate and was therefore a legitimate material property. The development of a macroscopic device capable of sensing the rheological response of microorganisms is a remarkable experimental achievement. It paves the way for the quantitative characterization of the flow behaviour of a wide range of microorganisms, and for understanding the role of different propulsion mechanisms.

Suspending non-motile particles in a fluid always increases the fluid's viscosity. Albert Einstein provided the first quantitative formulation of this intuitive effect in 1906 by showing that, in a dilute suspension of spheres, the increase in viscosity is linearly proportional to the volume fraction of suspended particles[13]. So how do swimming bacteria achieve the opposite effect and thin out the suspension, turning it into a frictionless liquid akin to a superfluid?

The answer relies on two key properties of flowing suspensions. First, inactive rod-like particles in an externally imposed shear flow align their long axes along the direction in which the flow 'stretches' the fluid. The rods tilt at a fixed angle that depends on their ratio of length to width; this angle can be close to 45° for long, slender rods (Fig. 1a). Many unicellular organisms, including *E. coli*, have such a rod-like shape and therefore orient in this way in shear flow.

Second, swimming bacteria exert forces on the surrounding fluids. These forces come in equal and opposite pairs: the force from the beating of their propulsive appendages (flagella or cilia) is balanced by the viscous drag on the cell's body. The spatial profile of these forces depends on the propulsion mechanism. Most bacteria use appendages mounted at the back of their bodies, and are known as pushers. When they move, they push fluid out at their front and back, while sucking it in at the sides.

Elongated pushers thus align their bodies along the stretching axis of the external flow and generate additional flows that further stretch the fluid in the same direction (Fig. 1b). At high enough concentrations, continuum theories suggest that the bacteria act collectively to push the fluid along, effectively thinning it. A microscopic understanding of how bacteria coordinate their response to shear to achieve a state of frictionless flow is still lacking. However, López and co-workers' experiments demonstrate that the viscosity of a suspension of swimming bacteria can indeed decrease with an increasing volume fraction of swimmers, within a range of bacterial concentrations.

By showing that bacteria can completely compensate for fluid friction by allowing the fluid to flow with zero dissipation, the authors have demonstrated that it is possible, in principle, to extract useful macroscopic mechanical power from bacterial activity. This observation is in line with earlier findings[14] that bacteria can work together to turn microgears. Although harnessing bacterial power for macroscopic energy generation may still be a dream, it is not such a stretch to imagine that bacteria could be used as mixers to thin and stir the flow in capillary and microfluidic devices. Quantitative characterizations of rheology of the type pioneered by López *et al.* pave the way to the development of bacterial baths tailored to mix and flow liquids for specific applications. ■

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ECOLOGY

Global trends in plant naturalization

Many naturalized non-native plants pose ecological and economic threats. A quantitative analysis of the global distribution of naturalized plants confirms some anticipated trends and exposes new patterns. SEE LETTER P.100

MARCEL REJMÁNEK

Naturalized species are non-native species that form self-sustaining populations following their introduction into an area by human agency[1]. Some naturalized species are considered a major threat to biodiversity and have been the focus of many biologists over the past three decades. However, even casual observers may notice that the distribution of naturalized species is highly uneven within and among different regions. Attempts to summarize global geographical distributions of naturalized organisms have included birds[2], ungulates[3] (large mammals such as pigs and camels) and bryophytes[4] (non-vascular plants), but a comprehensive assessment of naturalized vascular plants has been missing. In this issue, van Kleunen *et al.*[5] (page 100) provide the first global analysis of the numbers and distributions of naturalized vascular plants and their exchange between continents.

The authors used hundreds of data sources of various kinds to characterize the alien floras of 843 non-overlapping regions worldwide (481 mainland and 362 island areas). Characterization included the origin of the naturalized species and estimates of the numbers of native and non-native species per continent. The resulting database includes 13,168 plant species — 3.9% of the world's currently known vascular flora — that have become naturalized in at least one region. The authors suggest that this figure may be an underestimate, given the lack of data (or adequate data) for some regions.

One of the most striking results of this study comes from the authors' comparisons between large continental areas. These revealed that North America has accumulated the largest number of naturalized species of vascular plant (5,958), followed by Europe (4,140). This finding undoubtedly reflects more intensive introduction processes — both deliberate, for example for ornamental horticulture and erosion control, and accidental, as a result of frequent trade between these regions and the rest of the world.

Simple numbers of naturalized species do not, however, quantify the actual level of invasion. Previous work[6] has shown that, in North America, non-native species account for 51.3% of the 120 most widely distributed plant species, but account for only 2.1% in Europe. One possible explanation for the striking difference between Europe and North America is that the European flora, being part of the Eurasian flora, has been exposed to countless plant migrations over time, so that the resulting plant communities are less 'naive' and more resistant to new plant invasions. It is also likely that some European plant species have been selected for quick colonization of human-disturbed habitats, the habitats in which they are most often found naturalized in North America (Fig. 1).

Van Kleunen and colleagues' data also show that the Pacific Islands region exhibits the steepest increase in the cumulative number of naturalized species with respect to the total area involved. This result provides the first global verification of an expected pattern: that oceanic islands harbour more naturalized plant species than mainland areas of similar size. A primary reason for this may be that native communities on islands represent only a limited sample of the species that could potentially match the habitat, and they are therefore more open to the naturalization of introduced species.

At the same time, the data confirm previous preliminary analyses showing that continental regions with large tropical areas (Africa, South America, tropical Asia) have fewer naturalized plant species than predominantly temperate regions. Higher resistance to non-native species establishment, faster vegetation

50 Years Ago

It is probable that only those who have themselves been concerned with scientific research will appreciate all the fine nuances of Sir Cyril [Hinshelwood]'s address, but the picture he paints of the scientist as a creative worker, of the need for freedom of expression and appropriate conditions of work, and of public understanding if his work is to be fully effective, is intelligible to any layman. It is no picture of a scientist working and living in some 'ivory tower', or even of Thomson's Newton, "stemming alone vast eternity's unbounded sea", but rather of a happy voyager of strange seas of thought, in company with others trained in the same or many other disciplines.
From *Nature* 4 September 1965

100 Years Ago

In his presidential address, read at the Association of Museums, San Francisco, Dr. O. C. Farrington gave an able summary of the origin and evolution of natural history museums, which should be widely read in this country. More especially is this to be urged in view of the danger which threatens such institutions in the immediate future in regard to the policy of national retrenchment which is now in process of formation. There is a danger that the pruning-hook may be used too ruthlessly, thereby inflicting material harm. For reformers are generally enthusiasts, and therefore are to be carefully watched, experience having shown that a sense of proportion is not usually among their attributes. Museums, as he remarks, are even now commonly regarded as a luxury, but he leaves no uncertainty as to the vitally important part which the modern museum plays, and must continue to play, in ever-increasing force, in our national life.
From *Nature* 2 September 1915