of savant abilities are associated with autism, but exceedingly rarely, and not in the two brothers with the R451C polymorphism (*4*). Cognitive researchers may want to explore the appealing notion that alterations in neurexin-neuroligin complexes shift the balance of excitatory and inhibitory synapses to enhance learning and memory.

References

1. A. A. Chubykin *et al.*, *Neuron* **54**, 191 (2007).
2. H. Taniguchi *et al.*, *J. Neurosci*. **27**, 2815. (2007).
3. K. Tabuchi *et al.*, *Science* **318**, 71 (2007); published online 6 September 2007 (10.1126/science.1146221).
4. S. Jamain *et al.*, *Nat. Genet*. **34**, 27 (2003).
5. F. Volkmar, C. Lord, A. Bailey, R. T. Schultz, A. Klin, *J. Child Psychol. Psychiatry* **45**, 135 (2004).
6. D. H. Geschwind, P. Levitt, *Curr. Opin. Neurobiol.***17**, 103 (2007).
7. X. Zhao *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* **104**, 12831 (2007).
8. K. S. Kendler, R. J. Greenspan, *Am. J. Psychiatry* **163**, 1683 (2006).
9. A. M. Persico, T. Bourgeron, *Trends. Neurosci*. **29**, 349 (2006).
10. T. R. Insel, *Mamm. Genome,* **12**, 755 (2001).
11. L. J. Young, L. J. Pitkow, J. N. Ferguson, *Mol. Psychiatry* **7**, S38 (2002).
12. P. Levitt *Epilepsia* **46** (suppl. 7), 22 (2005).
13. C. M. Spencer *et al.*, *Genes Brain Behav.* **4**, 420 (2005).
14. M. Cheh *et al.*, *Brain Res.* **1116**, 166 (2006).
15. C. H. Kwon *et al.*, *Neuron* **4**, 377 (2006).
16. J. B. Panksepp, G. P. Lahvis, *Genes Brain Behav.* 10.1111/j.1601-183X.2006.00295.x (2006).
17. E. S. Brodkin, *Behav. Brain Res.* **176**, 53 (2007).
18. S. S. Moy *et al.*, *Behav Brain Res.* **176**, 4 (2007).
19. H. G. McFarlane *et al.*, *Genes Brain Behav.* 10.1111/j.1601-183X.2007.00330.x (2007).
20. H. C. Hazlett *et al.*, *Biol. Psychiatry* **59**, 1 (2006).
21. L. Zwaigenbaum *et al.*, *Int. J. Dev. Neurosci.* **23**, 143 (2005).

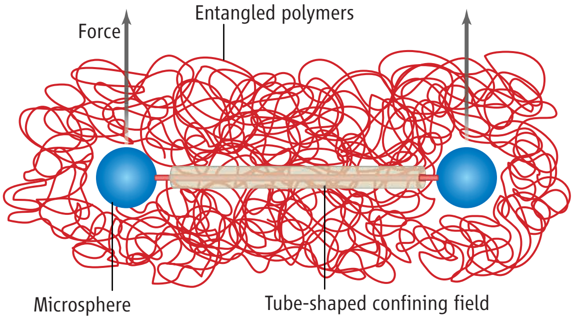
10.1126/science.1149801

BIOPHYSICS

Going with the Flow

A growing synergy between rheology and biophysics is yielding insights into the flow properties of polymers and biomolecules.

Ronald G. Larson



An insider view of entanglement. In (*9*), a probe DNA molecule was held stretched by two optically trapped microspheres in a solution of other DNA molecules. The confining tube potential (orange region) was explored by displacing the spheres perpendicular to the probe chain and measuring the resulting forces.

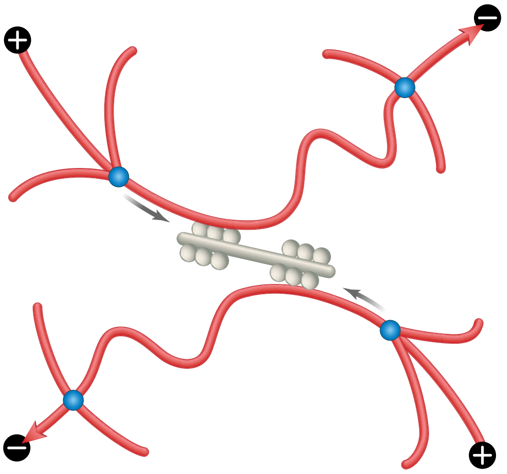
The field of rheology—the study of the deformation and flow of polymers, colloids, or emulsions—long had to content itself with macroscopic experiments, because the microstructures that produce the rheological response were beyond the reach of experimental tools. But now, new tools borrowed from biophysics allow these microscopic substructures to be probed directly, as illustrated by a recent use of optical tweezers to study the dynamics of entangled polymers (*1*). Another recent study exemplifies borrowing in the reverse direction: the use of a microrheological tool to study the actin filament network of a cell (*2*). These examples are just a small sampling of a growing synergy between rheology and biophysics that is yielding deeper understanding of the dynamics of biopolymers such as DNA and actin filaments and of conventional synthetic polymers such as polyethylene.

Since the mid-1990s, long double-stranded DNA molecules have been widely used to study the flow properties of polymers (*3*, *4*). Stained by intercalating dyes, double-stranded DNA molecules were visualized as they deformed, tumbled, stretched, and relaxed as a result of flow, yielding a thorough basis for understanding the flow behavior of dilute polymers (*5*–*8*).

However, dilute polymer solutions, in which the polymer molecules do not overlap, are rare in practical applications. Far more important are the higher-concentration regimes in which polymer molecules overlap and entangle with each other, as occurs, for example, when molten polyethylene is blown into plastic film or when silk solutions are spun by spiders into a thread.

Since the seminal work of de Gennes (*9*) and Doi and Edwards (*10*), theories for the rheology of densely entangled polymers have relied on the tube model. In this model, each polymer molecule is confined by entanglements with its neighboring molecules to a tubelike region that roughly follows the contorted, random-walk contour of the polymer molecule. Polymer motion is preferentially directed along this tube rather than perpendicular to it, with dramatic consequences for polymer dynamics and rheology. The tube model has remained largely phenomenological, with the properties of the confining tube determined only indirectly through observation of polymer motion and rheological properties. However, this may now be changing.

In a recent study, Robertson and Smith (*1*) attached small beads, which served as handles for optical traps, to both ends of a single long probe DNA molecule, which they mixed with a densely entangling solution of other, similar, DNA molecules (see the first figure). By stretching the probe molecule to nearly full extension using the traps and allowing surrounding molecules to relax, they created a straightened version of the tube. When both optical traps were displaced by the same



Motor-driven fluctuations. In (*12*), actin filaments (red) were pulled by ATP-powered myosin motors (gray) in the direction of the arrows. The resulting tensile forces are marked with (+); contractile forces are marked with (–). The cross-links (blue) link the mobile actin chains into a soft-solid network.

The author is in the Department of Chemical Engineering, University of Michigan, Ann Arbor, MI 48109, USA. E-mail: rlarson@umich.edu

CREDITS: (TOP) ADAPTED FROM (1); (BOTTOM) ADAPTED FROM (2)

Downloaded from www.sciencemag.org on October 5, 2007

Published by AAAS

amount perpendicular to the tube axis, the probe molecule was pressed into the entangling chains forming the "wall" of the tube (see the first figure).

By monitoring the slight deflections of the bead handles from the centers of their optical traps, the authors measured the forces exerted on the beads and hence on the probe molecule. The results indicate that the tube diameter slowly grows with time, as suggested by recent molecular dynamics simulations (*11*). Discoveries such as this are leading to a more refined understanding of entanglement interactions and should stimulate development of quantitative theories of entangled polymer dynamics and rheology.

While rheology has benefited from methods and tools borrowed from biophysical studies, microrheology tools developed for miniaturized rheological studies are used increasingly in biophysics. In conventional rheology, millimeter- or centimeter-size plates, cylinders, and other geometries are used to apply deformations and measure stress. In passive microrheology, these are replaced by thermal agitation, which spontaneously generates stress locally, with nanometer-scale deformation monitored by dynamic light scattering (*12*) or by laser interferometry (*2*). In active microrheology, optical traps are used to apply oscillatory forces onto probe particles, whose displacements then allow the frequency-dependent viscoelasticity of the micrometer-scale environment to be probed (*2*).

Originally applied to colloids, polymer solutions, and emulsions (*12*), versions of microrheology that use optical or atomic force microscopy are becoming prime tools for analyzing rheological behavior at the cellular and subcellular level in biology (*13*). For example, Mizuno *et al.* (*2*) recently used both active and passive microrheology to study networks of actin filaments interacting with myosin motors (see the second figure). At thermodynamic equilibrium, the frequency-dependent responses of active and passive methods were the same. However, in the presence of an energy source [in this case, adenosine 5′-triphosphate (ATP)], the active and passive methods yielded very different results at low frequency because of large nonequilibrium fluctuations driven by ATP hydrolysis. The motor-driven fluctuations also stiffened the actin network by a factor of 100. This finding may be of biological importance, because such networks form the "skeleton" of the cell, whose stiffness can be modulated through myosin motor activity, as demonstrated for a range of cells including stem cells (*14*).

Tools closely related to microrheology are likely to be used increasingly to manipulate single molecules of DNA and of the proteins that wrap, cleave, repair, unwind, copy, and transcribe the DNA (*15*, *16*). Likewise, new tools developed for studies of biopolymers and colloidal forces in the cell are likely to be applicable to a wide range of nonbiological fluids. Thus, the fruitful exchange of experimental and theoretical methods between the fields of biophysics and rheology is likely to continue.

References

1. R. M. Robertson, D. E. Smith, *Phys. Rev. Lett*. **99**, 126001 (2007).
2. D. Mizuno, C. Tardin, C. F. Schmidt, F. C. MacKintosh, *Science* **315**, 370 (2007).
3. T. T. Perkins, D. E. Smith, S. Chu, *Science* **276**, 2016 (1997).
4. C. Bustamante, J. F. Marko, E. D. Siggia, S. Smith, *Science* **265**, 1599 (1994).
5. E. S. G. Shaqfeh, *J. Non-Newt. Fluid Mech*. **130**, 1 (2005).
6. C. M. Schroeder, H. P. Babcock, E. S. G. Shaqfeh, S. Chu, *Science* **301**, 1515 (2003).
7. Y. L. Chen, M. D. Graham, J. J. de Pablo, K. Jo, D. C. Schwartz, *Macromolecules* **38**, 6680 (2005).
8. L. Fang, H. Hu, R. G. Larson, *J. Rheol*. **49**, 127 (2005).
9. P. G. de Gennes, *J. Chem. Phys*. **55**, 572 (1971).
10. M. Doi, S. F. Edwards, *Faraday Trans. II*. **74**, 1789 (1978).
11. Q. Zhou, R. G. Larson, *Macromolecules* **39**, 6737 (2006).
12. T. G. Mason, D. A. Weitz, *Phys. Rev. Lett.* **74**, 1250 (1995).
13. D. Weihs, T. G. Mason, M. A. Teitell, *Biophys. J.* **91**, 4296 (2006).
14. A. J. Engler, S. Sen, H. L. Sweeney, D. E. Discher, *Cell* **126**, 677 (2006).
15. N. R. Forde *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* **99**, 11682 (2002).
16. P. C. Blainey, A. M. van Oijen, A. Banerjee, G. L. Verdine, X. S. Xie, *Proc. Natl. Acad. Sci. U.S.A.* **103**, 5752 (2006).

10.1126/science.1142441

MATERIALS SCIENCE

There's Room in the Middle

Dense inorganic-organic hybrid materials offer opportunities for creating unusual properties or combinations of properties.

Anthony K. Cheetham and C. N. R. Rao

Condensed matter researchers have traditionally focused either on inorganic materials or on organic and bio-materials. Much less effort has been devoted to hybrid materials that contain both inorganic and organic components. This has changed in the past decade with the discovery of crystalline hybrid materials—called metal-organic frameworks or MOFs—that contain cavities and channels akin to those found in zeolites. Other recent discoveries include hybrid framework structures that are dense rather than porous, and systems that are more similar to classical inorganic materials.

Hoskins and Robson were among the first to combine molecular inorganic and organic building blocks to create open networks. The resulting topologies were often analogous to known inorganic structures such as diamond (*1*). Many other highly porous MOFs have since been synthesized (*2*, *3*). The properties of porous hybrid frameworks often resemble those of classical zeolites; for example, they can absorb gases and allow shape-selective catalysis. However, hybrid frameworks offer a wider range of structures and properties. For example, they can display chirally selective heterogeneous catalysis (*4*). Their electronic properties have also attracted attention (*5*).

Yet, apart from porous hybrid frameworks, the field has other opportunities to offer. Two aspects of the enormous structural diversity of hybrid framework materials deserve greater emphasis.

First, an increasing number of hybrids are being discovered in which the inorganic structural elements form an infinite array in one, two, or three directions (see the figure, top panel) (*6*–*9*). (In contrast, in MOFs, isolated metal ions or clusters are connected via organic linkers.) Infinite inorganic connectivity—for example, metal-oxygen-metal—provides the structural basis for many key physical properties of inorganic materials, such as ferromagnetism, metallic conductivity, and even superconductivity. These properties are thus likely to be found in hybrids of the kind shown in the top panel of the figure. Furthermore, they may be found in combination with other properties that result from the presence of the organic components.

Second, given that the overwhelming majority of functional inorganic materials adopt dense structures, greater attention

---

A. K. Cheetham is in the Department of Materials Science and Metallurgy, University of Cambridge, Cambridge CB2 3QZ, UK. C. N. R. Rao is at the Jawaharlal Nehru Centre for Advanced Scientific Research, Jakkur P.O., Bangalore 560 064, India. E-mail: akc30@cam.ac.uk; cnrrao@jncasr.ac.in

Downloaded from www.sciencemag.org on October 5, 2007

Published by AAAS