



Spare the (Elastic) Rod Philip C. Nelson *Science* **337**, 1045 (2012); DOI: 10.1126/science.1227014

This copy is for your personal, non-commercial use only.

If you wish to distribute this article to others, you can order high-quality copies for your colleagues, clients, or customers by clicking here.

Permission to republish or repurpose articles or portions of articles can be obtained by following the guidelines here.

The following resources related to this article are available online at www.sciencemag.org (this information is current as of November 28, 2012):

Updated information and services, including high-resolution figures, can be found in the online version of this article at: http://www.sciencemag.org/content/337/6098/1045.full.html

A list of selected additional articles on the Science Web sites **related to this article** can be found at: http://www.sciencemag.org/content/337/6098/1045.full.html#related

This article cites 14 articles, 4 of which can be accessed free: http://www.sciencemag.org/content/337/6098/1045.full.html#ref-list-1

This article appears in the following **subject collections:** Biochemistry http://www.sciencemag.org/cgi/collection/biochem

Science (print ISSN 0036-8075; online ISSN 1095-9203) is published weekly, except the last week in December, by the American Association for the Advancement of Science, 1200 New York Avenue NW, Washington, DC 20005. Copyright 2012 by the American Association for the Advancement of Science; all rights reserved. The title *Science* is a registered trademark of AAAS.

~10 nm

BIOCHEMISTRY

Spare the (Elastic) Rod

Philip C. Nelson

hysicists love emergence. From a welter of complex details about a system's constituents, simple and universal rules sometimes emerge that adequately describe the collective behavior of the components. Even if these rules are not completely universal, they often have only a few relevant parameters, a vast simplification compared to the many that describe the constituents individually. But as Vafabakhsh and Ha remind us on page 1097 of this issue (1), emergent behavior can conceal important aspects of a system. Using a beautiful application of fluorescence microscopy, the authors provide the clearest evidence to date that the elasticrod model for DNA mechanics, an emergent description that works well on long length scales, breaks down on shorter length scales relevant to cell biology.

Emergence is often a function of increasing length scale. For example, the complex intermolecular dynamics of individual water molecules can be ignored in the design of plumbing; for this purpose, it suffices to know just two parameters for water: its mass density and its viscosity.

However, the very forgetfulness of nature that simplifies its long-scale character can also conceal the details that we need to know if we are to understand shorter-scale regimes.

Department of Physics and Astronomy, University of Pennsylvania, 209 South 33rd Street, Philadelphia, PA 19104, USA. E-mail: nelson@physics.upenn.edu

The mechanical properties of DNA are a case in point. It is tempting to regard this famous molecule as just a database containing the algorithm for constructing an organism. But DNA is also a physical object that constantly bends, twists, and interacts with other biomolecules. Particularly important, DNA is often observed to be tightly bent, in contexts such as gene regulation and packaging (see the figure).

Polymer physicists have long known that a stiff polymer like DNA will display emergence. On long length scales, such a molecule may be adequately described as an elastic rod, that is, a rod that resists bending with a linear relation (Hooke's Law). The mathematics of elastic rods was developed in the 19th century; all that is needed in the polymer context is to add the action of random thermal motion, which takes on crucial importance on the nanometer scale.

Some of the first single-molecule manipulation experiments on DNA found that the simple elastic rod model, despite having only a single free parameter, gave a quantitative account of the behavior of lambda phage DNA (2). This agreement became even more impressive with later experiments.

Could DNA be literally regarded as a linearly elastic rod? The late Jonathan Widom (3) did not think so. He knew that the rod model required a prohibitive amount of elastic energy to be expended to form the strucExperiments show that at biologically relevant length scales and under conditions resembling those in cells. DNA does not behave like an elastic rod.

PERSPECTIVES

tures shown in the figure; yet, these structures form readily.

To reduce uncertainties that arise from the complex cellular milieu, Cloutier and Widom undertook in vitro experiments with DNA fragments of length equal to the circumference of the nucleosome core particle. They assayed the ability of these fragments to form loops in the absence of the histone proteins that might be thought to facilitate loop formation. The results were astonishing. Not only did small loops form readily; for loops of biologically relevant sizes (see the figure), the ability to form spontaneously was found to be nearly independent of loop size (apart from a modulation with periodicity equal to the helical pitch) (4, 5).

Perhaps these results should not have come as a great surprise. It has long been known that DNA has discrete alternate conformations, attainable at a modest free-energy cost, including some with sharply localized kinks (6), locally melted regions, and flipped-out base pairs. Thus, just as bending a soda straw eventually gives a catastrophic breakdown of its rod elasticity, so too could severe nonlinearities enter DNA elasticity. Kinks were also known to form in tightly bent structures like the nucleosome (7, 8). Accordingly, immediately after Cloutier and Widom's work, theorists investigated simple models incorporating highly bendable behavior on short length scales (9, 10). Such models automatically

~50 nm



small capsid. The results of Vafabakhsh and Ha bear on the question of how such structures can self-assemble despite the high elastic energy cost traditionally attributed to tightly bent DNA.

С

displayed emergent elastic-rod behavior on long length scales, thus reconciling the new experiments with the old ones. Later, a mesoscopic (intermediate-scale) model was found that incorporated still other experimental results, yet, like the original elastic rod, had only one free parameter (11).

Unfortunately, Cloutier and Widom's experiments were fraught with uncertainties. Their assay relied on the large ligase enzyme, required an intricate protocol, and did not directly report looping rates. Later experiments have given similar results without use of ligase (11, 12), but in each case, some aspect of the assay did not resemble the situation in vivo.

Vafabakhsh and Ha now offer a clean, simple demonstration of non-rodlike behavior in DNA at biologically relevant scales. The new work is done in vitro, and hence is free from many unknowns in the cell, yet was not affected by some potential artifacts present in previous in vitro experiments, for example, the proximity of hard walls and large reporter beads. Not only do their results vindicate Widom's intuition; they also show that this behavior occurs for generic sequences [it is even more pronounced for special ones (13)]. Finally, the experiment confirms the near independence of looping ability on DNA length in the relevant regime—a cardinal property in the theories of (9-11).

The new results will still need to be integrated with previous experiments, not all of which have seemed to fit the picture described above (14). They will also provide guidance as theory seeks to go beyond generic models to ones predicting the details of sequence dependence. Already, however, they illustrate the two-edged character of emergence: It can simplify behavior, but this is not always appropriate. To learn about a system on some length scale, we must devise experiments that specifically probe that particular scale.

References

(2010)

- 1. R. Vafabakhsh, T. Ha, Science 337, 1097 (2012).
- C. Bustamante, J. F. Marko, E. D. Siggia, S. Smith, *Science* 265, 1599 (1994).
- 3. R. Phillips, Nature 476, 400 (2011).
- 4. T. E. Cloutier, J. Widom, Mol. Cell 14, 355 (2004).
- T. E. Cloutier, J. Widom, Proc. Natl. Acad. Sci. U.S.A. 102, 3645 (2005).
- 6. F. H. Crick, A. Klug, Nature 255, 530 (1975).
- M. E. Hogan, T. F. Rooney, R. H. Austin, *Nature* **328**, 554 (1987).
- 8. T. J. Richmond, C. A. Davey, Nature 423, 145 (2003).
- 9. J. Yan, J. F. Marko, Phys. Rev. Lett. 93, 108108 (2004).
- P. A. Wiggins, R. Phillips, P. C. Nelson, *Phys. Rev. E Stat. Nonlin. Soft Matter Phys.* **71**, 021909 (2005).
- 11. P. A. Wiggins *et al.*, *Nat. Nanotechnol.* **1**, 137 (2006). 12. L. Han *et al.*, *PLoS ONE* **4**, e5621 (2009).
- 13. S. Johnson, M. Lindén, R. Phillips, Nucleic Acids Res.
- (2012); 10.1093/nar/gks473. 14. J. P. Peters III, L. J. Maher, *Q. Rev. Biophys.* **43**, 23

10.1126/science.1227014

CHEMISTRY

Vibrational Excitation Can Control Tropospheric Chemistry

Which products form during the oxidation of acetylene by hydroxyl radicals and oxygen depends on the internal excitation of a radical intermediate.

Geoffrey Tyndall

arth's atmosphere is often compared to a low-temperature combustion system. Reactive hydrocarbons are emitted from both natural and anthropogenic sources and then oxidized by hydroxyl radicals (OH) through a complex chain of reactive free radicals. It is usually assumed that the molecules and radicals involved are all in their lowest energy states. However, on page 1066 of this issue, Glowacki et al. (1) show that a strikingly different product distribution can be obtained in the oxidation of acetylene depending on whether the radicals contain high amounts of internal (vibrational) energy or are fully relaxed. The study used a combination of experiment and theory to provide a complete description of the reaction of OH radicals with acetylene in the presence of varying amounts of O₂ and N₂.

Acetylene (C_2H_2) is an important atmospheric constituent, being emitted as a byproduct of incomplete combustion. It has an atmospheric lifetime of about 12 days (which is governed by its reaction with OH radicals), which allows it to be used as a tracer of anthropogenic activity or biomass burning in relatively clean regions. Previous studies have shown that two sets of oxidation products are accessible under atmospheric conditions: one makes formic acid and formyl radicals, and the other makes glyoxal and reforms the hydroxyl radical (see the figure). The overall reaction rate constant was measured a number of years ago (2,3) but during one of these studies, Bohn et al. (2) noted that the apparent rate constant for OH loss was reduced in the presence of oxygen. To explain the O_2 dependence of the rate constant, they suggested that the O_2 could interact with the energetic free radicals (R-OH) produced from the addition of OH to acetylene. Glowacki et al. convincingly confirmed this hypothesis by both experiments and theory.

Acetylene is a linear molecule with a triple bond between the carbon atoms. When OH adds to C_2H_2 , the hydrogen atom on the opposite carbon can end up either on the same side as the OH or diametrically opposed. According to the calculations of Glowacki *et al.*, the configuration with the hydrogen furthest from the oxygen should

be the most stable and leaves an unpaired electron next to the oxygen (the cis position). When O_2 adds to this unpaired electron, it can easily abstract the H atom on the OH group, providing a low-energy exit channel to glyoxal and OH. If the O_2 adds trans to the hydroxyl group, the rearrangement to products is a little more tortuous, but should also be rapid, leading to formic acid and HCO.

The two conformations of the radical do not interchange freely in the ground state but are separated by a small energy barrier. However, when the OH initially adds to the C_2H_2 , the intermediate radicals have sufficient internal energy (in the form of vibrational excitation) such that the hydrogen can flip easily between the cis and trans configuration. However, collisions with other molecules transfer energy out of the radical, and after a sufficient number of collisions, the internal energy is reduced below the barrier. Thus, the more energetic the C_2H_2 -OH radical is when it reacts with O_2 , the more likely it is to produce formic acid, and vice versa.

The situation acquires added complexity when it is recognized that O_2 can act both as a collision partner and a reactive partner, whereas N_2 just acts as an inert collision

31 AUGUST 2012 VOL 337 **SCIENCE** www.sciencemag.org *Published by AAAS*

National Center for Atmospheric Research, 3090 Center Green Drive, Boulder, CO 80301, USA. E-mail: tyndall@ ucar.edu