is pressed into a polymer film. The films are monodispersed polystyrenes with average molecular masses of 9000 kD, 900 kD, and 44 kD, with corresponding R_g values of approximately 84 nm, 26 nm, and 6 nm, respectively, in the bulk melt state (R_g scales with the square root of molecular mass). The film thickness, h, is varied from 170 nm to 36 nm, becoming thinner than the R_g of the highest-molecular-mass polystyrenes. The authors argue that the rheological response where the thickness of the film is strongly confining relative to the diameter of the molecule is relevant to an NIL imprint where the mold cavity is smaller than the R_g of the polymer.

The results are striking. For thick films ($h >> R_g$), the resistance to the large-strain deformation of the polymer melt increases substantially with the molecular mass of the polystyrene, consistent with the bulk viscosity. However, when the film thickness is smaller than the radius of gyration, both the contact modulus (the resistance to small-scale elastic deformation) and the forming stress (the load required to induce large-scale plastic deformation) are strongly reduced. For the polystyrene with the highest molecular mass (9000 kD) in the 36-nm film, which is approximately one-half the bulk R_g, both the forming stress and large-strain deformation resistance are smaller than for the lowest-molecular-mass polystyrene (44 kD) of the same thickness. This thickness is still about 6 times the bulk R_g for the 44-kD polystyrene and is therefore presumably less confined.

Why such a dramatic reduction of the forming stress and flow resistance in high-molecular-mass polymers relative to the bulk viscosity? The large-strain properties of polymers are dominated by the topological entanglements of the transient network established by the interpenetrating polymer coils (*6*). For chains at surfaces, at interfaces, and in thin films, it has been suggested that the interface acts as a reflecting plane. The polymer coil is not allowed to cross the boundary, so it must "reflect" and remain within the confines of the interface (*7*–*9*). Small-angle neutron scattering measurements on thin polymer films have shown that the R_g in the plane of the film is unaffected by thin-film confinement (*10*). This means that when the film thickness decreases and starts to compress the coil in the vertical direction, the polymer does not respond by spreading laterally in-plane (see the figure). Rather, the chain folds back on itself at the film interface, resulting in the chain segment's nearest neighbors belonging to the same chain, thus decreasing the degree of coil-coil interpenetration (*11*).

These arguments are provocative given the strong correlation between entanglement and melt rheology. A loss of entanglement would seem to facilitate flow in polymer thin films. Although this has been very difficult to prove, the experimental results of Rowland *et al.* provide some of the strongest evidence to date to support this argument. Si and co-workers (*12*) used tensile deformation measurement of glassy polystyrene to deduce a loss of entanglement in thin polymer films, which seems to support the reports of facilitated flow here. However, there are also compelling reports from bubble inflation (*13*) and surface force (*14*) measurements of polymer melts "stiffening" in very thin films. How this problem unravels is not only a scientifically intriguing question, but is also of technical relevance as manufacturing processes such as NIL evolve to fabricate nanoscale features from relatively gigantic molecules.

References

1. J. D. Ferry, *Viscoelastic Properties of Polymers* (Wiley, New York, ed. 3, 1980).
2. H. D. Rowland, W. P. King, J. B. Pethica, G. L. W. Cross, *Science* **322**, 720 (2008); published online 2 October 2008 (10.1126/science.1157945).
3. S. Y. Chou, P. R. Krauss, P. J. Renstrom, *Science* **272**, 85 (1996).
4. S. H. Ahn, L. J. Guo, *Adv. Mater.* **20**, 2044 (2008).
5. Y. F. Ding *et al.*, *Adv. Mater.* **19**, 1377 (2007).
6. M. S. Green, A. V. Tobolsky, *J. Chem. Phys.* **14**, 80 (1946).
7. E. A. DiMarzio, *J. Chem. Phys.* **42**, 2101 (1965).
8. H. R. Brown, T. P. Russell, *Macromolecules* **29**, 798 (1996).
9. L. J. Fetters, D. J. Lohse, D. Richter, T. A. Witten, A. Zirkel, *Macromolecules* **27**, 4639 (1994).
10. R. L. Jones, S. K. Kumar, D. L. Ho, R. M. Briber, T. P. Russell, *Nature* **400**, 146 (1999).
11. P. G. de Gennes, *Scaling Concepts in Polymer Physics* (Cornell Univ. Press, Ithaca, NY, 1979).
12. L. Si, M. V. Massa, K. Dalnoki-Veress, H. R. Brown, R. A. L. Jones, *Phys. Rev. Lett.* **94**, 4 (2005).
13. P. A. O'Connell, G. B. McKenna, *Science* **307**, 1760 (2005).
14. H. W. Hu, S. Granick, *Science* **258**, 1339 (1992).

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ECOLOGY

Physiology and Climate Change

Studies of physiological mechanisms are needed to predict climate effects on ecosystems at species and community levels.

Hans O. Pörtner[1] and Anthony P. Farrell[2]

Ongoing ecosystem changes in response to climate change include poleward or altitudinal shifts in geographical distribution (*1*–*3*), population collapses or local extinctions (*4*), failure of large-scale animal migrations (*5*), changes in the seasonal timing of biological events (*6*), and changes in food availability and food web structure. These changes are largely driven by environmental temperature (*1, 7*). Examples from aquatic animal communities show that study of physiological mechanisms can help to elucidate these ecosystem changes and to project future ecological trends.

All organisms live within a limited range of body temperatures, due to optimized structural and kinetic coordination of molecular, cellular, and systemic processes. Functional constraints result at temperature extremes. Increasing complexity causes narrower thermal windows for whole-organism functions than for cells and molecules, and for animals and plants than for unicellular organisms (*8*). Direct effects of climatic warming can be understood through fatal decrements in an organism's performance in growth, reproduction, foraging, immune competence, behaviors and competitiveness. Performance in animals is supported by aerobic scope, the increase in oxygen consumption rate from resting to maximal (*9*). Performance falls below its optimum during cooling and warming. At both upper and lower pejus temperatures, performance decrements result as the limiting capacity for oxygen supply causes hypoxemia (*4*, *8*) (see the figure, left). Beyond low and high critical temperatures, only a passive, anaerobic existence is possible. Fish rarely exploit this anaerobic range, but invertebrates inhabiting the highly variable intertidal environment use metabolic depression, anaerobic energy production, and stress protection mechanisms to provide short- to medium-term tolerance of extreme temperatures.

Thermal windows likely evolved to be as narrow as possible to minimize maintenance costs, resulting in functional differences, between species and subspecies in various climate zones (*10*–*12*) and even between populations of a species (*13*); for example, the

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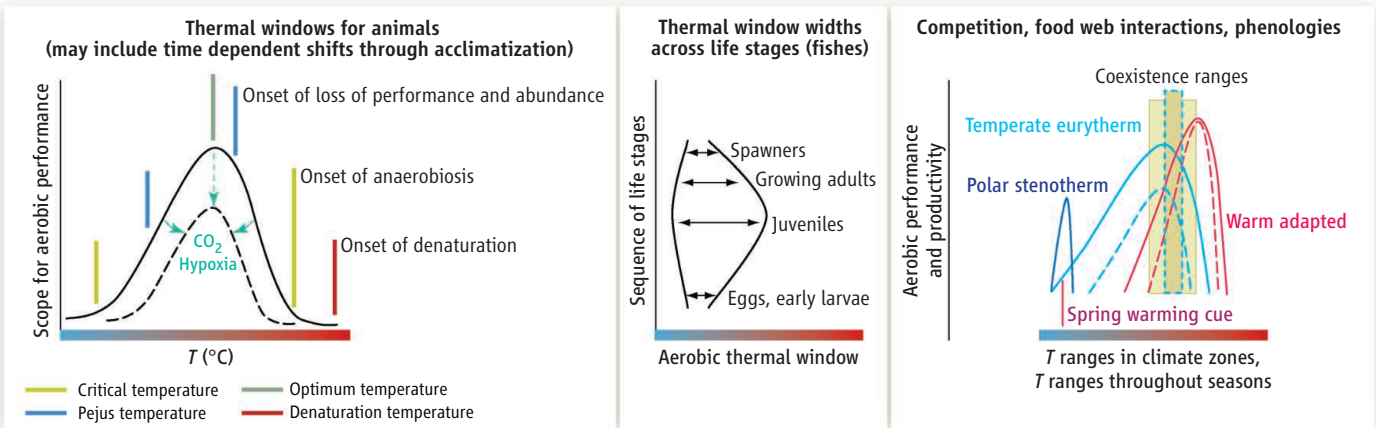

Temperature effects on aquatic animals. The thermal windows of aerobic performance (**left**) display optima and limitations by pejus (pejus means "turning worse"), critical, and denaturation temperatures, when tolerance becomes increasingly passive and time-limited. Seasonal acclimatization involves a limited shift or reshaping of the window by mechanisms that adjust functional capacity, endurance, or protection (*4*). Positions and widths of windows on the temperature scale shift with life stage (**middle**). Acclimatized windows are narrow in stenothermal species, or wide in eurytherms, reflecting adaptation to climate zones. Windows still differ for species whose biogeographies overlap in the same ecosystem (**right**, examples arbitrary). Warming cues start seasonal processes earlier (shifting phenology), causing potential mismatch with processes timed according to constant cues (light). Synergistic stressors like ocean acidification (by CO_2) and hypoxia narrow thermal windows according to species-specific sensitivities (broken lines), modulating biogeographies, coexistence ranges, and other interactions further.

optimal and critical temperatures differ by 2° to 3°C between two sockeye salmon populations from the Fraser River in British Columbia, Canada (*5*).

Long-term fisheries data revealing climate impacts on fish stocks have often been related to food web effects. However, they can also involve direct warming impacts on individual species, linked to thermal windows. For example, in the German Wadden Sea, growth and abundance of a nonmigratory eelpout decreased when summer maximum temperatures surpassed the upper pejus temperature, with larger individuals affected first (*4*). In the Japan Sea, different thermal windows between sardines and anchovies for individual growth, gamete production and quality, and spawning activity caused a regime shift to anchovies in the late 1990s (*14*, *15*). In the Fraser and Columbia River systems, warming has often delayed spawning migrations of nonfeeding Pacific salmon, potentially causing loss of fitness (*16*). Cardiac collapse above the critical temperature likely brought on swimming failure and mortality among Fraser River sockeye in 2004 (*5*).

The ongoing northward shifts of North Sea Atlantic cod stocks likely involve both direct effects on cod and indirect food web effects. Clear correlation of these shifts with winter warming indicates greatest sensitivity of the fishes during their winter reproductive period (*1*). One reason may be that the oxygen demand of a 20% gonadal mass (*17*) disadvantages mature females by narrowing their thermal window (see the figure, middle). Also, the enhanced reproductive capacity of large body size reduces optimal temperatures for growth and increases heat sensitivity (*13*). Furthermore, thermal windows for growing larval fish, which might be as narrow as those of reproducing adults, may also reflect limited oxygen supply, when the developing ventilation and circulatory systems take over from simple diffusion across the body surface.

An indirect effect of warming is implied in the shifted community composition in the Southern North Sea from larger to smaller zooplankton prey (*18*), reducing the food available to juvenile cod. This shift likely reflects different thermal windows for these copepod species as well as for cod and their prey, given that oxygen-limited thermal tolerance was recently confirmed for small zooplankter (*19*). Such differences between windows may, in general, underpin changes in species interactions and cause shifts in spatial or temporal overlap (see the figure, right).

Further ecosystem-level responses to climate change include shifts in the seasonal timing of recurring processes (*20*). Earlier seasonal development of zooplankton or its grazing later in the year may no longer match the timing of phytoplankton blooms (*6*). Climate could elicit such shifts when warming cues enter or leave thermal windows earlier in the year (see the figure, right). As other cues like seasonal light conditions remain constant, this may cause previously matched species interactions to go out of phase; food availability may change.

Extending the principle of specialization on differing thermal windows to interacting species can help explain changing biogeographies, community composition, and food web structures. These changes mostly set in at the borders of current distributions, where species operate at the limits of their thermal windows; acclimatization mechanisms fail to maintain performance and shift thermal limits further. Such trends can be compensated for by evolutionary selection for adequate genotypes. However, such adaptation may be too slow for long-lived species. Climate change will thus differentially favor species with wide thermal windows, short generation times, and a range of genotypes among its populations.

Carbon dioxide, hypoxia, salinity change, and eutrophication contribute to ecosystem responses to climate change (*21*). Key to setting sensitivity to ocean acidification are the mechanisms and efficiency of systemic acid-base regulation (*22*). Such specific effects of each stressor will reduce whole-organism performance, especially at extreme temperatures, thereby narrowing thermal windows and reducing biogeographical ranges. Studies of ecosystem consequences of stressors like ocean acidification through carbon dioxide should thus consider effects on thermally limited oxygen supply. The principles elaborated here may also be applicable to organisms other than animals and to both aquatic and terrestrial ecosystems (*23*).

References

1. A. L. Perry, P. J. Low, J. R. Ellis, J. D. Reynolds, *Science* **308**, 1912 (2005).
2. K. Brander *et al.*, *ICES Mar. Sci. Symp.* **219**, 261 (2003).
3. J. M. Grebmeier *et al.*, *Science* **311**, 1461 (2006).
4. H. O. Pörtner, R. Knust, *Science* **315**, 95 (2007).

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5. A. P. Farrell *et al.*, *Physiol. Biochem. Zool.* **81**, 697 (2008).
6. K. H. Wiltshire, B. F. J. Manly, *Helgol. Mar. Res.* **58**, 269 (2004).
7. C. Rosenzweig *et al.*, *Nature* **453**, 353 (2008).
8. H. O. Pörtner, *Comp. Biochem. Physiol.* **132 A**, 739 (2002)
9. J. R. Brett, *Am. Zool.* **11**, 99 (1971).
10. H. O. Pörtner, *Deep Sea Res. II* **53**, 1071 (2006).
11. N. A. Fangue, M. Hofmeister, P. M. Schulte., *J. Exp. Biol.* **209**, 2859 (2006).
12. J. H. Stillman, *Science* **301**, 65 (2003).
13. H. O. Pörtner *et al.*, *Climate Res.* **37**, 253 (2008).
14. A. Takasuka, Y. Oozeki, I. Aoki, *Can. J. Fish. Aquat. Sci.* **64**, 768 (2007).
15. A. Takasuka, Y. Oozeki, H. Kubota, *Mar. Ecol. Prog. Ser.* **360**, 211 (2008).
16. T. M. Goniea *et al.*, *Trans. Am. Fish. Soc.* **135**, 408 (2006).
17. R. Dahle, G. L. Taranger , Ø. Karlsen, O. S. Kjesbu, B. Norberg, *Comp. Biochem. Physiol.* **136 A**, 641 (2003).
18. P. Helaouët, G. Beaugrand, *Mar. Ecol. Progr. Ser.* **345**, 147 (2007).
19. O. Pinkhaus *et al.*, *Freshw. Biol.* **52**, 1537 (2007).
20. M. Winder, D. B. Schindler, *Ecology* **85**, 2100 (2004).
21. J. M Guinotte, V. J. Fabry, *Ann. N.Y. Acad. Sci.* **1134**, 320 (2008).
22. H. O. Pörtner, M. Langenbuch, B. Michaelidis, *J. Geophys. Res.* **110**, C09S10, 10.1029/2004JC002561 (2005).
23. J. J. Tewksbury, R. B. Huey, C. A. Deutsch, *Science* **320**, 1296 (2008).

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CANCER

Aneuploidy Advantages?

The gain or loss of specific chromosomes can determine whether a cell becomes tumorigenic.

Eva Hernando

The role of aneuploidy—the presence of an abnormal number of chromosomes—in cancer has been at the center of debate for almost a century. Although aneuploidy is a hallmark of most tumor cells, whether it is a cause or a consequence of the malignant transformation (oncogenesis) has not been clear. In 1914, German biologist Theodor Boveri postulated that aneuploidy arising from altered cell division (mitosis) might lead to oncogenesis. However, recent studies with genetically modified organisms have kept the issue open to argument. Certain defects in chromosome segregation during mitosis that lead to aneuploidy can either promote (*1*, *2*) or inhibit tumor formation (*2*, *3*), or even have no effect at all (*4*). On page 703 in this issue, Williams *et al.* (*5*) provide an interesting twist, by showing that harboring an extra chromosome may or may not drive a mammalian cell into oncogenesis, depending on the chromosome itself and on the state of the cell.

Earlier studies reported the deleterious effects of aneuploidy during human development (causing miscarriages) and in adulthood (underlying mental retardation). The findings of Williams *et al.* are compatible with this view, showing that having an abnormal number of chromosomes is initially disadvantageous for mammalian cells. The authors cultured mouse cells that were engineered to express a specific additional chromosome (trisomy). These cell lines had decreased rates of proliferation, and increased cell size and metabolic rates, all conditions that reduce cell fitness. However, in some cases, these limitations could be overcome. The ability of a cell line to proliferate indefinitely in culture (immortalization) depended on the identity of the extra chromosome. Certain chromosome gains accelerated the attainment of immortalization, whereas others delayed or impaired it.

To what extent do these in vitro results reproduce the survival pressure that somatic cells undergo in vivo, and their capacity to adapt to stressful conditions? The mouse embryonic fibroblasts used by Williams *et al.* have higher spontaneous immortalization rates than other primary mouse or human cells in culture. Do the effects of aneuploidy in these fibroblasts occur in other cell types from which most common tumors arise? Also, the elegant strategy of chromosomal translocation used by the authors to simulate increased chromosome numbers may not strictly represent all forms of aneuploidy, nor fully recapitulate, from a structural standpoint, the gain or loss of individual chromosomes.

In any case, Williams *et al.* propose that certain gains or losses of specific chromosomes are more compatible with cell viability than others, thus explaining the variable effects of chromosome gains observed in the mouse cells. Thus, in a normal cellular context—that is, in the absence of mutations that predispose a cell for transformation—aneuploidy alone seems an unlikely driver of oncogenesis. But in a procancerous context, aneuploidy could promote malignant cell transformation. This hypothesis could be tested by introducing aneuploidy in immortalized (not yet transformed) cell lines.

What are the advantages conferred by aneuploidy in a permissive context? Although initially less proliferative, aneuploid cells are inherently unstable, and thus endowed with increased genomic instability and mutational rate. This may lead them to acquire the hallmarks of cancer, such as resistance to cell

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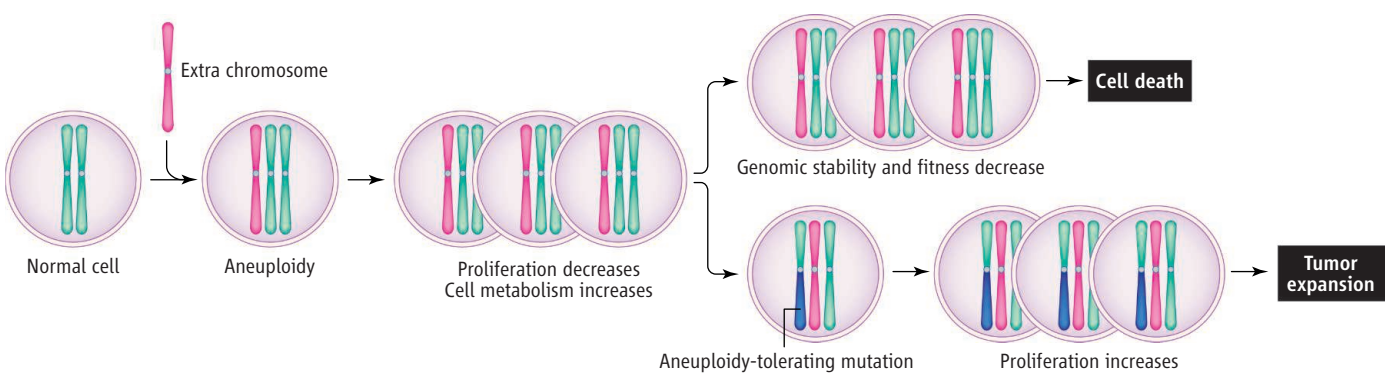

Gains and losses. According to the aneuploidy model of Williams *et al.*, an abnormal chromosome number may be costly to cell fitness. However, if mutations arise that allow the cell to adapt to cellular imbalances caused by the abnormal chromosome content, cells may eventually form tumors.

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