

The question that puzzles me is not how *Phoberomys* could have been so large, but why the overwhelming majority of rodents are so small. Would giant rodents perhaps be more vulnerable to predators than faster running ungulates? Small mammals commonly escape predators by retiring into a refuge such as a burrow. The fairly short

limbs typical of rodents combined with paws for digging would be of benefit for this mode of escape. Large mammals, too big to burrow, can generally escape only by running. Ungulates—with their long legs, light hooves, and long elastic tendons—seem best for that. Would large rodents generally be too slow to be successful?

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AGING

It's Never Too Late

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Experiments in species as diverse as yeast, worms, flies, and rodents demonstrate that dietary restriction prolongs survival. The encouraging findings of Mair *et al.* (1) on page 1731 of this issue now reveal that a lifetime of abstemiousness is not required to reduce one's risk of death—at least in fruit flies. These investigators show that when flies fed a restricted diet are switched to a full diet, mortality soars to the level suffered by fully fed flies. Conversely, when the diet of fully fed *Drosophila* is restricted, mortality plunges within 2 days to the level enjoyed by flies that have experienced a lifelong restricted diet.

The alliterative title of the Mair *et al.* paper—"Demography of Dietary Restriction and Death in *Drosophila*"—gives due credit to demography as the source of their new discovery. Demographers have long realized that death rates provide age-specific information that cumulative survival curves cannot (2). Heeding this insight, Mair *et al.* analyzed the daily mortality of their fed and hungry flies. Demography offers a further lesson: Death of the frail alters the composition of a cohort, lowering subsequent mortality and possibly offsetting increases in mortality resulting from cumulative damage (3).

Replication and refinement of Mair *et al.*'s experiments especially in rodents, the principal animal model of dietary-restriction studies, will be a research priority. Rodent and *Drosophila* dietary-restriction experiments differ in two key respects. First, rodents in these experiments cannot mate or produce offspring because they are maintained in solitary confinement or in same-sex cages. Mair *et al.* allowed their

flies to mate before separating them into containers holding about 100 females or 200 males. They did not report egg production, but it seems likely that fully-fed females lay many eggs whereas females on restricted diets lay few (4). Even in all male containers, fully-fed males may have engaged in behavior associated with attracting females (such as courtship songs composed of wing vibrations) to a greater extent than males on restricted diets. Hence, Mair *et al.*'s findings could be due to a switch in and out of costly reproductive activity, but evidence for this will require further study.

Second, in rodent experiments, diets are restricted by reducing food quantity (generally to 60% or ad libitum), whereas in

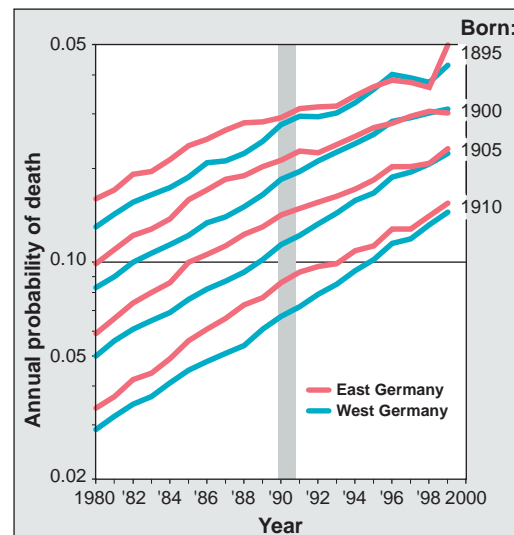
Drosophila experiments, the effect is achieved by reducing food quality. In their study, Mair *et al.* cut the yeast and sugar content of the fly diet to about 43% of that in standard laboratory medium. Other work in Mediterranean fruit flies (medflies) (5) shows that reductions in food quantity do not increase longevity (6), whereas reductions in food quality do (7). A key uncertainty is whether quantity- or quality-restricted diets or ad libitum diets mimic conditions in the wild.

Mair *et al.*'s findings are important not only in the context of dietary-restriction research but also from the broader perspective of what determines longevity. Demographers have shown that age-specific death rates for humans are strongly influenced by current conditions and behaviors. Mortality, even at advanced ages, is highly plastic. This is well illustrated by the "natural experiment" of German unification, analogous to the laboratory experiments of Mair and colleagues.

Following unification of East and

West Germany (1989–1990), mortality in the East declined toward prevailing levels in the West, especially among the elderly (8, 9) (see the figure). Although conditions early in life do significantly influence human health and survival late in life (10), the German example—and other demographic data—provide strong evidence that such effects are of less importance (at least in more recent decades) than changes in current conditions (2, 11, 12). The second half of the 20th century saw a radical (and continuing) decline in old-age mortality in most developed countries: in Western Europe, for instance, from 1950 to 2000 the probability of surviving from age 80 to 100 increased 20-fold (13). Most of this increase is due to improvements in economic and social conditions and to ongoing medical advances (14).

Epidemiological and clinical research provide further evidence of the malleability of old age. For example, the risk of death for elderly smokers who quit falls, within 1 or 2 years, to a lower level than that suffered by recalcitrant smokers (15).



East and West German death rates for cohorts born

around 1900. The Berlin Wall fell on 9 November 1989 and formal unification of East and West Germany was completed on 3 October 1990 (gray column). Before 1989, the annual probability of death was considerably higher in East Germany compared with West Germany for cohorts born in 1895, 1900, 1905, and 1910. In 1990, people born in these years were in their 80s and 90s. Nonetheless, very old East Germans were able to benefit from medical, social, and economic improvements after unification. Consequently, their death rates converged toward those of West Germany.

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There is a growing appreciation that even octogenarians and nonagenarians can substantially benefit from medical interventions such as cataract surgery (16) and hip replacement (17). Low-tech interventions at advanced ages can have an important impact. For instance, Fiatarone *et al.* found that physical training leads to significant gains in muscle strength, size, and functional mobility among frail residents of nursing homes: The oldest person studied (and helped) was 96 years old (18).

Aristotle contrasted premature death with natural death due to old age—he asserted that nothing could be done about old age (19). More than 23 centuries later, many still believe that death rates at older ages are intractable (20). This view is reinforced by evolutionary theories of aging, which emphasize that senescence is inevitable because the force of selection against deleterious, late-acting mutations declines with age (21). Research over the past decade strongly supports an encouraging alternative—that aging is plastic and survival can be substantially extended by various genetic changes and nongenetic interventions (1–2, 5, 7–18, 20). For most species, damage to cells and tissues accu-

mulates with age, and mortality rises. Nonetheless, aging is so remarkably pliable that interventions do not have to be life-long. As illustrated by the Mair *et al.* report and other studies, interventions even late in life can switch death rates to a lower, healthier trajectory.

Are there any limits to the extraordinary malleability of aging? Will an article in *Science* soon report that various genetic changes and nongenetic interventions can help nematode worms, *Drosophila*, or medflies (which ordinarily live a few weeks at most) to survive more than a year? Since 1840, record life expectancy has increased by 2½ years per decade (20). Will this march to longevity continue for many more decades? What genetic mechanisms and physiological processes determine the malleability of aging? Why does evolution license it? These are the kinds of questions that will spur future mortality research.

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MATERIALS SCIENCE

Polymers Go with the Flow

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The flow of polymers, either as melts or in solution, shows some intriguing features. Polymeric liquids climb stirrer rods (the Weissenberg effect), swell up at the exit of an extruder or capillary, and can even sustain tubeless siphons (1, 2). These phenomena cannot be explained by classical hydrodynamics. Yet they are typical of most polymeric substances, independent of their chemical composition. On page 1691 of this issue, Bent *et al.* (3) show that theoretical understanding of this “universal” behavior has advanced so far that it can quantitatively reproduce the properties of a complex flow similar to those encountered in applications.

The generic behavior of polymers must arise from the chainlike structure of the polymer molecules, but detailed insights into the underlying processes have been hard to come by. Until the 1980s, polymer flow could only be described phenomenologically by fitting the observed behavior through suitable (yet arbitrary) nonlinear

extensions of the Boltzmann equation of linear viscoelasticity. Early molecular approaches were successful only in addressing the dynamics of an isolated chain in a sea of solvent (4, 5). The resulting Rouse-Zimm theory worked well for dilute solutions but was clearly inadequate for concentrated solutions and for most melts.

The Rouse model (4) replaces the polymer chain by a sequence of friction beads connected by springs. Predictions from this model match the observed behavior of polymer melts of low molecular mass, but fail completely at higher masses. The failure was correctly ascribed to the presence of “entanglements”: Long, concentrated polymers in the liquid state intertwine with one another, and hence their dynamics are strongly influenced by the constraint that the chains cannot cut across one another in their motion.

The first important step toward solving the entanglement problem was taken by Edwards (6), who introduced the “tube” as a mean-field description of the topological confinement exerted on a given chain by the surrounding chains (see the figure, panel A). Next, de Gennes (7) solved a fundamental aspect of the entangled dy-

namics by describing the diffusion of a chain along its own length, a process that he named “reptation” (panel B). Finally, Doi and Edwards (8, 9) developed a full theory of the entangled state of liquid polymers by combining the idea of the tube with reptation. Their theory explicitly encompassed not only thermal motion but also forced motion due to flow. Further refinements by various authors included tube end fluctuations, constraint release due to thermal motion of the surrounding chains (panel C), and chain stretch under very fast flows (panel D) (10).

The resulting theory was successful in many respects and appeared intuitively convincing, but there remained a very important drawback. The theory predicted an excessive shear thinning that would cause highly unstable flow. This feature was not only unrealistic, but also completely precluded simulation of the complex flows encountered in applications. The way out of this dilemma was found much later (11), when it was recognized that one important dynamic factor had been overlooked: convective constraint release, which becomes dominant in fast flows. Subsequent developments (12, 13) made it possible to achieve the success reported by Bent *et al.* (3). In today’s theoretical picture, the tube experiences a Rouse-like motion due to constraint release (panel C), both thermal and convective, while the chain within the tube un-

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