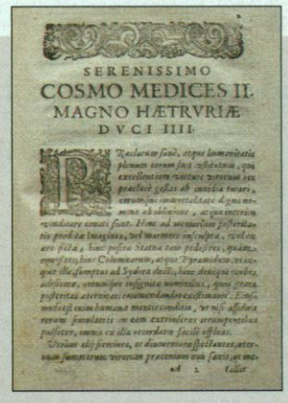
genes, the evolution of pleiotropy, the accumulation of modifier mutations, and so on. The authors themselves brand the chapter "conceptual meanderings." But it is one thing to meander, another to synthesize. This lack of coherence lends the book a diffuse, unrigorous quality and is, in the end, its most serious problem. Now and then the clash of ideas gets so bad that the text slips into unintelligibility, as when we are told, "The innate complexity of genetic systems necessarily leads to emergent properties arising from epigenetic processes that integrate the output components of myriad local genetic programs into a functional global phenotype." Such talk seems an unlikely first step to clearer understanding.

Phenotypic Evolution is representative of a popular trend—some pet theory (take your pick: plasticity, development, complexity theory, or chaos) gets elevated to its rightful place as "the" way to think about evolution. But this longing to dress up biology in unusual new perspectives has, so far, yielded more book deals than results. Although new ways of thinking will surely be required in the attempt to unravel the genetical evolution of the phenotype, considerable care and taste are needed in their selection. Schlichting and Pigliucci's confused admixture is not the perspective we have been waiting for.

NOTA BENE: CD-ROMS

To Read and Enjoy



Galileo Galilei's *Sidereus Nuncius* (1610) has been called the most earthshaking book published in the history of astronomy. In this work, Galileo defined a modern view of the universe and our place in it. His most important observation—that Jupiter was at the center of what appeared to be a mini–planetary system—simultaneously demonstrated that the sun and humankind were not foci of the heavens. Benjamin Franklin's *Experiments and Observations on Electricity* (1751) is one of the most important treatises of the 18th century because of its systematic approach to a physical phenomenon. The rarity and fragility of these original documents have for centuries put them out of reach for all but a very select, privileged few. Thanks to digitizing technology and Adobe's Acrobat Reader, however, we now can scroll page-by-page through carefully scanned original versions of these fascinating works. Other significant historic scientific books also available on CD-ROMs (and as downloadable Acrobat files) from Octavo Corporation (Oakland, CA; www.octavo.com) include Nicholas Copernicus' *De Revolutionibus Orbium Coelestium* (1543), Robert Hooke's *Micrographia* (1664), William Harvey's *Exercitatio Anatomica de Motu Cordis et Sanguinis in Animalibus* (1628), and Isaac Newton's *Opticks* (1704).

The detail and beauty of these documents in full color is breathtaking. One can see the texture of the pages, down to the actual indentations made by the metal type on the original paper and the inevitable marks and colorings of age. Users can "thumb through" the books as many times as desired without worrying about damaging fragile pages. Complete English translations are provided where appropriate, and computer search tools allow the reader to easily locate text of interest. Best of all, the modest price of the products ($25 to $75) enables virtually anyone with access to a computer to view these classic volumes in all of their original glory.

—KEVIN AHERN

CREDIT: *SIDEREUS NUNCIUS*/OCTAVO CORPORATION

PERSPECTIVES: CELL CYCLE

The Difficulty in Separating Sisters

Terry L. Orr-Weaver

One of the defining events during cell division (mitosis) is the separation of sister chromatids that are attached to each other and to the mitotic spindle, a process called cohesion release. But we are only now beginning to understand how the powerful cohesive forces that hold the sister chromatids together are overcome. In the budding yeast, *Saccharomyces cerevisiae*, the chief player seems to be the Esp1 protein—a so-called separin—which is also found in human cells, raising the possibility that the mechanism of cohesion release is highly conserved (*1*). On page 418 of this issue, Zou *et al.* add another piece to the puzzle with their report that an oncogene, *PTTG* (pituitary tumor-transforming gene), acts as a regulator of Esp1. This suggests that defective regulation of cohesion may contribute to cancer by promoting chromosome instability (*2*). Like a classic murder mystery plot, the prime suspect for "doing in" sister-chromatid cohesion, the anaphase-promoting complex (APC), now turns out to be a mere accomplice, with the less colorful Esp1 character actually responsible for the deed.

Physical association of the sister chromatids is crucial for their stable attachment to microtubules from opposite spindle poles and for their proper segregation at the transition from metaphase to anaphase. Cohesin, a conserved multiprotein complex, is essential for the tight association of the sister chromatids, which is established as the DNA is replicated during S phase (*3*). The cohesin complex is localized along the length of the sister chromatids and, as shown by a report in last week's *Science*, is also bound to the centromere (the constricted area of the chromosome to which spindle microtubules bind) (*4*). In budding yeast, two cohesin subunits, Scc1p (also called Mcd1p) and Scc3p, dissociate from the chromatids at the onset of anaphase, coinciding with release of cohesion.

Ubiquitin-mediated proteolysis is necessary to activate the transition from metaphase to anaphase. The APC tags mitotic cyclins with a ubiquitin marker, targeting them for degradation; the cells are then able to exit mitosis. The APC also has other substrates that must be degraded to ensure sister-chromatid separation (*5*). The initial theory that the APC directly releases cohesion by degrading cohesin was disproved by the finding that cohesin subunits persisted into telophase, the final step of cell division (*6, 7*). Rather, it turned out that APC triggers the degradation of a group of proteins called securins that inhibit sister-chromatid separation. Securins include Pds1p in *S. cerevisiae* and a different protein, encoded by the *cut2*

The author is at the Whitehead Institute and the Massachusetts Institute of Technology, Cambridge, MA 02142, USA. E-mail: weaver@wi.mit.edu