wechsel (leading tone exchange), green], which generate a dihedral group of order 24, isomorphic to the group of rotations and reflections of a 12-sided polygon. Each transformation exhibits efficient voice leading, preserving two pitch classes and moving the third by a small interval; arrows always cross dotted lines of the same color. The Beethoven progression (highlighted in the graph and expanded at the bottom of the figure) unfolds a PL-cycle that circumnavigates the torus, starting and ending in B-flat major, and illustrates that the composite transformation PLPLPL is the identity element of the group.

The Tonnetz is only one of many possible geometric representations of musical spaces (*11*), and recent studies have extended neo-Riemannian methods to larger and more powerful transformation groups, to other chord types besides triads, and in various other directions (*12*). In addition to group theory and other algebraic techniques, ideas from graph theory, combinatorics, geometry, and topology have found musical application. The work of Tymoczko *et al.* embraces all of these strategies in an innovative and wide-ranging investigation of chordal space. One of the great attractions of this work is its generality: It aims to describe what is in effect a "space of all chords" wherein the Tonnetz and many other familiar depictions of musical relationships appear as subspaces, projections, and cross sections. The spaces appearing here are of a type known as orbifolds, as they possess singularities—points where the geometry is not locally Euclidean. (The appeal to the recent topological concept of orbifolds is notable in a field that relies mainly on mathematics of a more classical vintage.) Other valuable contributions include a fresh perspective on the elusive notions of consonance and dissonance, connections between symmetries of the spaces and various musical practices, and many implications for the efficient chord-to-chord voice leading that has long been considered a hallmark of successful composition.

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DEVELOPMENTAL BIOLOGY

Morphing into Shape

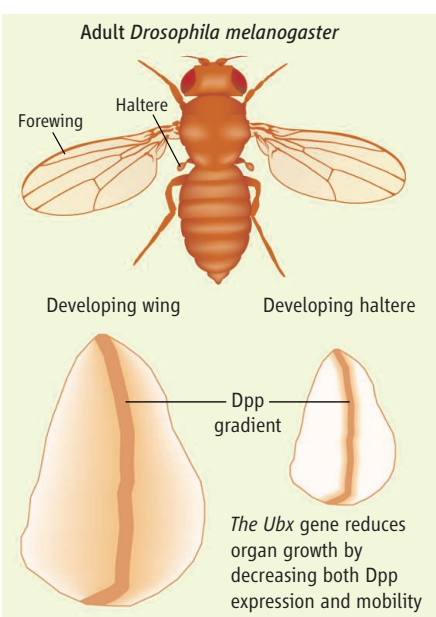
David L. Stern

Two appendages of the fly, the haltere and the wing, grow to very different sizes. Limited expression and mobility of a growth morphogen is partly responsible for this difference.

In 1917, British polymath D'Arcy Thompson proposed that the shapes of different organisms—say, a human and a chimpanzee—could be imagined as simple alterations of the same underlying pattern (*1*). Thompson famously demonstrated this idea by overlaying transformed Cartesian coordinates on drawings of related animals. This holistic view of organism shape inspired the British biologist Julian Huxley to point out that changes in shape can be thought of most simply as differences in the relative sizes of different body parts, thus reducing shape change to a more manageable problem (*2*). On page 63 of this issue, Crickmore and Mann (*3*) present a detailed analysis of the mechanisms controlling one striking difference in the relative size of two organs and uncover what may be a general mechanism of shape evolution.

In segmented organisms, such as flies and humans, similar structures that differ mainly in size and shape are produced in several locations along the main body axis. For example, humans produce arms and legs, largely using many of the same developmental mechanisms to pattern both organs. In fruit flies, two flying appendages, the wings and halteres (see the figure), also are built largely by shared developmental mechanisms. Halteres are delicate club-shaped organs that work like gyroscopes during flight. They evolved about 225 million years ago from more traditional-looking wings—such as the hind wings of butterflies—and have undergone a drastic reduction in size.

All of the differences between the wing and the haltere are determined by expression of a single "selector" gene called *Ultrabithorax* (*Ubx*), which is expressed in all cells of the developing haltere. When *Ubx* is experimentally removed from these cells, a fully formed wing grows instead of a haltere (*4*), revealing some of the underlying similarities between the two flight organs. *Ubx* somehow instructs other genes to alter the growth and development of haltere cells. In 1998, Weatherbee *et al.* (*5*) showed that *Ubx* regulates a battery of genes in the haltere, but until now we have not known precisely which genes are regulated to cause the greatest difference between the wing and the haltere: their fivefold difference in cell number in the adult.



How is organ size controlled? The *Ubx* gene is expressed in haltere cells, restricting the growth effect of the morphogen Dpp during development.

Crickmore and Mann focused their attention on how *Ubx* influences the activity of *decapentaplegic* (*dpp*), a gene that is one of the key regulators of wing growth. Dpp protein is produced by cells that lie in a line that is several cells wide along the middle of both the wing and the haltere. The protein is then secreted from these cells and diffuses to neighboring cells. When the Dpp protein binds to its receptor, Thickveins (Tkv), two things happen. First, a signal is triggered within the cell and this signal is interpreted as "grow more." Second, the Dpp protein is captured by the cell and eventually destroyed. Thus, Dpp protein diffuses away from the central cells and forms a gradient whose extent and steepness is controlled, at least in part, by the receptor Tkv.

Crickmore and Mann first noted that the width of the stripe of cells producing Dpp was narrower in the haltere than in the wing, and the level of expression per cell was also lower in the

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haltere. That is, less Dpp is produced in the haltere. Remarkably, they also found that the receptor Tkv is expressed in different patterns and amounts in the wing and in the haltere. In the central part of the wing, Tkv expression is low, allowing the Dpp protein to move far from its source and creating two peaks of Dpp signaling on either side of the Dpp source. In the haltere, by contrast, all cells express high levels of Tkv, thus trapping Dpp close to the source and creating a narrow band of cells that respond to the Dpp signal. The result of all of this is that, relative to the haltere, more cells in the wing are exposed to the Dpp signal and they proliferate more than haltere cells.

Evolution appears to have hijacked an existing mechanism of growth control when flies evolved halteres. *Ubx* directs halteres to be smaller than wings by regulating multiple points in the Dpp pathway. It is remarkable that both the amount of the growth signal and the distance it is allowed to travel have come under the control of *Ubx*. Crickmore and Mann note that similar changes would provide an elegant mechanism for altering organ shape and size in different species. There is already evidence that changes in the expression of *Bmp4*, a relative of the *dpp* gene, in Darwin's finches are correlated with changes in the shape of the finches' beaks (*6*).

So how general is this mechanism? Molecules such as Dpp that transmit information through a field of cells in a graded manner are called morphogens. It is easy to imagine, given the data presented by Crickmore and Mann, that evolutionary alterations in the production and transport of morphogens through fields of cells could explain much of the geometric diversity observed by D'Arcy Thompson. Whether this is in fact the usual manner in which organ shape and overall shape evolve remains to be seen.

One particular difficulty is how this phenomenon scales to larger sizes. Morphogens tend to act over distances of tens of cells. It is difficult to imagine that tweaking a morphogen signal can lead to the differences between a fruit fly wing and a butterfly wing, or between a mouse and an elephant. Perhaps larger animals make larger organs by tinkering with morphogen gradients, or perhaps they generate new domains of morphogen activity. They may also have adopted an entirely different process that communicates with mechanisms controlling overall body size. There has recently been considerable progress in understanding how the insulin signaling pathway and other hormones (*7*, *8*) control body size in animals, but there is as yet little clarity about how morphogens and hormones intersect. It is nonetheless clear from the work of Crickmore and Mann that modification of the production and transport of morphogens may provide evolution with at least one powerful and flexible tool for altering organism shape.

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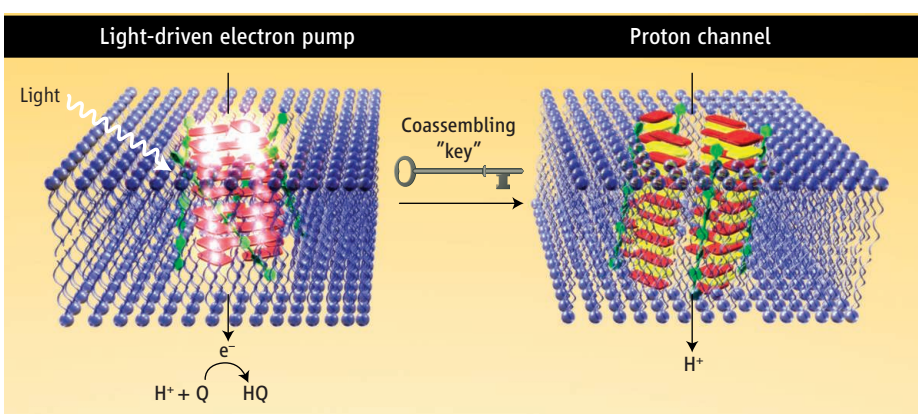
CHEMISTRY

From Electron Pump to Proton Channel

Artificial chemical systems can mimic biological ones and pump electrons across membranes in response to light. They can also be engineered to exhibit other desirable features.

Kazushi Kinbara and Takuzo Aida

Hydroelectric power generation uses the potential energy stored in dammed water. When an upstream gate is opened, the downstream flow of water drives a turbine to generate electric power. Such energy storage and release systems are also important at nanometer dimensions in cells and biological machines, where molecules control all the events involved. On page 84 of this issue, Bhosale *et al*. extend these concepts to a fully synthetic system (*1*). By integrating a self-assembled molecular gate into a vesicular membrane, they demonstrate an elegant proton-consuming and -refilling system (*1*). When the gate is closed, it serves as a light-driven electron transport pathway; when the gate is open, it forms an ion channel. Addition of a molecule serves as a key for opening the gate (see the figure).



Generation and release of a concentration gradient of protons. Transformation of a light-driven electron pump (**left**) into an ion channel (**right**) is triggered by an externally added molecule that serves as a key. Q, quinone derivative; HQ, hydroquinone derivative.

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At a molecular level, energy can be gained from fluxes of substances along their concentration gradient. Many biological events, including flagellum rotation, signal transduction, and muscle contraction, make use of this mechanism to generate their driving energy. In biological systems, protons, Na^+, K^+, or Ca^{2+} ions are concentrated on one side of a biomembrane by the action of chemical "pumps." When certain channels are constructed in the biological membrane, unidirectional flows of these ions take place. Some biological membranes, such as thylakoid membranes, contain light-harvesting chromophore arrays that enable the use of light energy for generating a concentration gradient of protons.

Ever since Kunitake (*2*) and Ringsdorf (*3*) pioneered the development of artificial liposomes (vesicular assemblies of amphiphilic molecules), researchers have tried to realize energy