BIOLOGY

Some Respect, Please, for the Glorious *Drosophila*

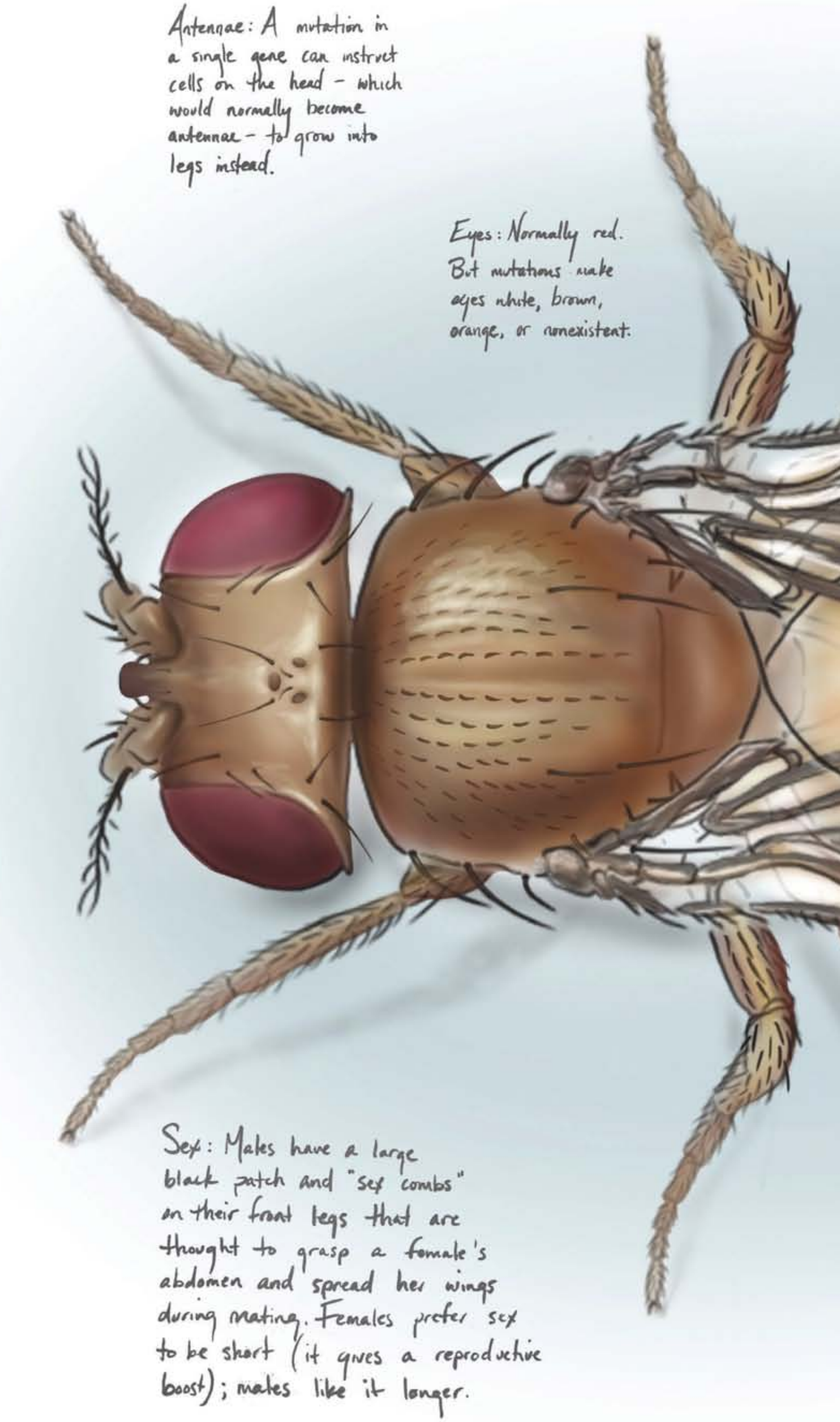
Hate those pesky fruit flies? Think again

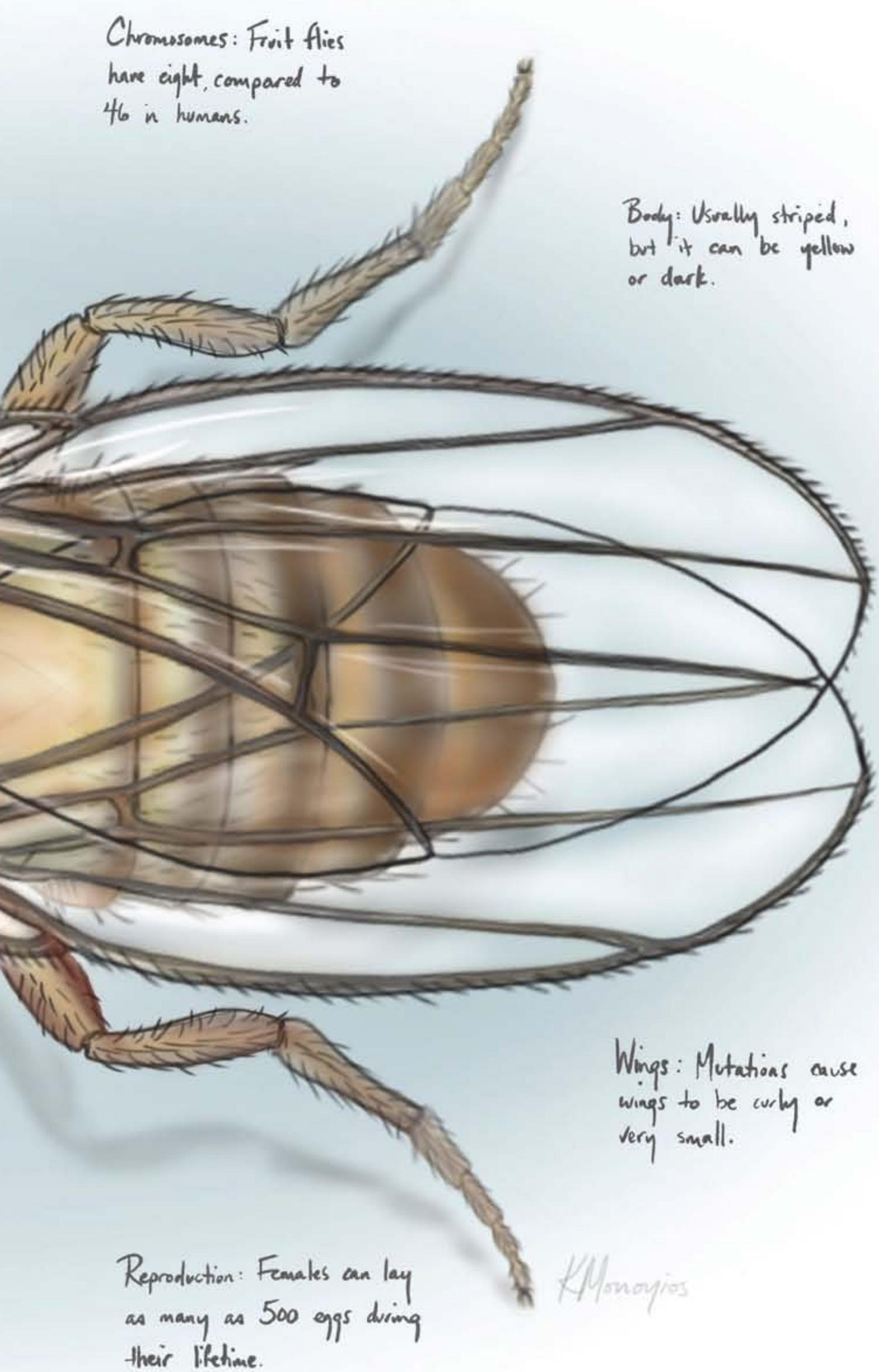
If you're one of those people who runs for a can of Raid after finding a swarm of fruit flies hovering over the ripe bananas in your kitchen, consider this: For more than a century, scientists have come to understand some of the most important processes taking place in the human body by studying these flies.

Ask any fruit-fly researcher why he or she works on this tiny insect — its proper name is *Drosophila melanogaster* — and the initial answer is likely to be "genetics." Evolutionary biologist Thomas Hunt Morgan started the tradition by using a mutant strain of the fruit fly to study heredity, showing that genes are linked in a linear arrangement on chromosomes and are responsible for specific hereditary traits. His work was key in establishing the field of genetics — and in elevating *Drosophila* to laboratory stardom. It earned Morgan the Nobel Prize in 1933.

Scientists have continued to identify flies with mutations just by looking at them — different eye and body colors, curly rather than straight wings, and extra wings. These characteristics then are linked to a gene mutation to figure out the gene's function.

Princeton's best known fly researcher, molecular biology professor Eric





Wieschaus, received the Nobel Prize in medicine in 1995 for identifying genes that regulate embryonic development. "We basically just did genetics, randomly knocking out genes and looking to see the consequences," says Wieschaus. He and colleagues screened hundreds of thousands of mutant embryos. The approach, he says, was based on the idea that since there are so many genes (the fruit-fly genome has more than 14,000), it would be useful to understand how they work together in a network.

Scientists have used the flies to study health issues, including Alzheimer's disease.

The genes Wieschaus found to control patterning and organ development in the fruit fly have since been shown to be the same genes that control similar processes in humans. While scientists may take genetics for granted now, in the 1970s it was not yet fully understood that "genetics could be a tool to understand life," he says.

Scientists have used the flies to study health issues, including those related to aging, Alzheimer's disease, and diabetes. The fly provides a window into things like circadian rhythm, drug addiction, and Parkinson's disease. Most of the major signaling pathways essential for human development — the routes through which information flows in cells — that were found to be mutated in cancer first were discovered in the fly.

The flies are cheap to raise (a container with a ripe piece of fruit would do the trick) and multiply quickly: A pair of flies produces more than 200 offspring. It takes only 12 days for a fly to grow from an egg to a 3-mm-long adult, so scientists can experiment quickly. Wieschaus now is working to understand the physical properties of cells: how they move and change shape. His research subject, of course: humble, glorious *Drosophila*. ◆ *Anna Azvolinsky *09*

What are Princeton researchers studying with fruit flies? Turn to the next page.

VIEW: Images of fruit fly embryos and more at **paw.princeton.edu**

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They Rely on the Fly

Much of the progress in medicine and human health has resulted from basic science and the search to understand life at a fundamental level: how normal cells function, how genes are expressed, and how cells communicate with one another. These professors, among others, use *Drosophila melanogaster* in this work. Here's what they're studying:

Peter Andolfatto, ecology and evolutionary biology and the Lewis-Sigler Institute for Integrative Genomics Only a small portion of the genome is made up of genes that become proteins. The other 82 percent of the fruit fly's DNA (98 percent in humans) control how and where genes are expressed. Studies using the fruit fly by Andolfatto and others were among the first to show that portions of this so-called "junk" DNA have important functions. This is now being confirmed in the human genome. By sequencing the genomes of fruit flies found in nature, rather than those raised in the lab, Andolfatto studies how the genome is shaped by adaptive evolution.

Thomas Gregor, physics and the Lewis-Sigler Institute for Integrative Genomics While other scientists study how the fertilized egg creates a body plan of its future self in the first few hours of development, "we are now putting a quantitative, physics layer on top," says Gregor — measuring the molecules in live embryos to determine how and why the fly's development is so precise and reproducible. Using special microscopes and other tools developed in his laboratory to measure these molecules, Gregor has shown that there is much more precision in the early stages of embryo development than previously thought.

Elizabeth Gavis, molecular biology Gavis seeks to understand how the pattern of the embryo is set up during development of the egg and early embryo. Her lab has developed a system to fluorescently label molecules to watch their movements in live eggs and embryos. She has shown that the asymmetric placement of these molecules tells the fruit fly which end will turn into the head and which will become the tail end. Some of the same molecules are needed for fertility in mammals.

Paul Schedl, molecular biology How are the 6 billion base pairs of the human genome (about 2 meters of DNA if stretched end to end) packed into a space of 6 micrometers? And how does the cell access this genomic information to express genes? The answer: DNA is combined with proteins to form a structure called chromatin, and different chromatin parts are organized into open and closed sections for ease of use. Schedl studies elements of fruit-fly chromatin that arrange genes into open or closed sections or switch them between the two.

Gertrud M. Schüpbach, molecular biology Fertilization of the fruit-fly egg kicks off the complicated process of forming an embryo. It turns out that much of the information and some of the building blocks needed for the embryo to develop are placed in the eggs when they are being made in the ovaries, rather than coming from the newly formed embryo genome. Schüpbach studies how this happens. ◆ *Anna Azvolinsky *09*

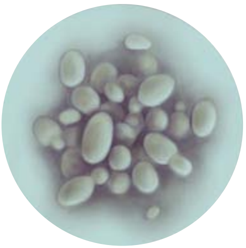
Loved in the Lab

The fruit fly has competition when it comes to popularity. Here are three others on researchers' hot lists:

THE ROUNDWORM
(*Caenorhabditis elegans*) A single fertilized egg develops into a transparent 959-celled, 1-mm-long nematode in just three days, making it easy to observe its development under the microscope. The worms are inexpensive to grow and require only bacteria as a source of food. Behavioral changes during the worm's lifespan of two to three weeks allow researchers to tell a young worm from an old one, making *C. elegans* a great tool to study aging, as does Professor Coleen Murphy.

THE ZEBRAFISH
(*Danio rerio*) Like humans, these tropical freshwater fish are vertebrates with a spinal cord, brain, and major organs. Unlike humans, one zebrafish pair produces as many as 300 embryos per day, making genetic studies fast and relatively easy. The embryos are large, grow outside of the mother, and are transparent, so development can be observed directly. Scientists are using the fish to study processes and diseases such as muscular dystrophy; Professor Rebecca Burdine uses them in research related to congenital heart defects.

BAKER'S YEAST
(*Saccharomyces cerevisiae*) Though it has only one cell, it still is a eukaryote, an organism whose genetic material is encased in a nucleus. Scientists' understanding of how cancer cells deviate from normal cells came from first studying these processes in yeast. "In one day, we can grow a flask of yeast cells that contains many more individual organisms than the number of human beings that have ever been on Earth," says Professor Mark Rose, who uses yeast to better understand fertilization.



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