Fruit fly research may 'clean up' conventional impressions of biology

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The metamorphosis of biology into a science offering numerically precise descriptions of nature has taken a leap forward with a Princeton team's elucidation of a key step in the development of fruit fly embryos -- discoveries that could change how scientists think not just about flies, but about life in general.

While biologists have long known that the structure of adult animals follows a blueprint laid out in the early stages of embryonic development, classical biological experiments have provided only isolated "snapshots" of the development process, denying scientists a complete "movie" of it unfolding.

Now, by combining experimental methods from physics and molecular biology, the team has replaced these snapshots with the movie, allowing them to see the first steps of blueprint formation in the fly embryo literally live and in color. The first of two papers in the July 13 issue of the scientific journal *Cell* describes the sophisticated techniques required to make these movies, techniques that could help scientists investigate a wide variety of biological systems.

In the second paper, the group poses a new question, never before asked by scientists studying embryos: How precisely can cells in the embryo read the blueprint"

So precisely, the paper suggests, that a precious few molecules signaling a change can make a decisive difference.

"I think the prevailing view has been that cells accomplish all their functions using a complicated combination of mechanisms, each one of which is rather sloppy or noisy," said team member William Bialek, the John Archibald Wheeler/Battelle Professor in Physics. "This research, however, indicates that in the initial hours of a fly embryo's development, cells make decisions to become one part of the body or another by a process so precise that they must be close to counting every available signaling molecule they receive from the mother."

Three hours into a fly embryo's development, it remains a single large cell with an unusual characteristic: Unlike other cells, which have a single nucleus, the embryo has thousands, each of which awaits a signal from the mother to form itself into a specialized cell. This signal arrives in the form of a droplet of protein called Bicoid that enters the embryo at one end and, like food coloring in water, diffuses out molecule by molecule through the nuclei. The concentration decreases with distance and forms the first blueprint that defines which part of the embryo will become the head and which the backside of the fly.

The team's findings indicate that two neighboring nuclei can determine their different places and functions within the embryo accurately if the concentration of Bicoid between them varies by only about 10 percent -- a quantity that on the scale of the tiny embryo amounts to only a few molecules of Bicoid.

"This signaling requires a sensitivity approaching the limits set by basic physical principles," Bialek said. "Perhaps more important than the answers we have found so far, this work has led us to sharpen the kinds of questions we ask about living cells as we try to understand them with the same kind of mathematical precision that we understand the rest of the physical world."

Source: Princeton University