

Researchers build largest protein interaction map to date

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Researchers have built a map that shows how thousands of proteins in a fruit fly cell communicate with each other. This is the largest and most detailed protein interaction map of a multicellular organism, demonstrating how approximately 5000, or one third, of the proteins cooperate to keep life going.

"My group has been working for decades, trying to unravel the precise connections among the proteins and gain insight into how the [cell functions](#) as a whole," says Spyros Artavanis-Tsakonas, Harvard Medical School professor of [cell biology](#) and senior author on the paper. "For me, and hopefully researchers studying [protein](#) interactions, this map is a dream come true."

The study is published October 28 in the journal *Cell*.

While genes are a cell's data repository, containing all the instructions necessary for life, proteins are its labor force, talking to each other constantly and channeling vital information through vast and complicated networks to keep life stable and healthy. Humans and [fruit flies](#) are both descended from a [common ancestor](#), and in most cases, both species still rely on the same ancient [cellular machinery](#) for survival. In that respect, the fruit fly's map serves as sort of a blueprint, a useful guide into the [cellular activity](#) of many higher organisms.

Understanding how proteins behave normally is often the key to their disease-causing behaviour.

For this study, Artavanis-Tsakonas and his colleagues provide the first large-scale map of this population of proteins. Their map, which is not yet fully complete, reveals many of the relationships these myriad proteins make with each other as they collaborate, something which, to date, has been to a large degree an enduring mystery among [biologists](#).

"We already know what approximately one-third of these proteins do," Artavanis-Tsakonas said. "For another third of them we can sort of guess. But there's another third that we know nothing about. And now through this kind of analysis we can begin to explore the functions of these proteins. This is giving us extraordinary insight into how the cell works."

One significant use for such a map is to assess how a cell responds to changes in metabolic conditions, such as interactions with drugs or in conditions where genetic alterations occur. Finding such answers might lead to future drug treatments for disease, and perhaps to a deeper understanding of what occurs in conditions such as cancer.

"This is of extraordinary translational value," Artavanis-Tsakonas said. "In order to know how the proteins work you must know who they talk to. And then you can examine whether a disease somehow alters this conversation."

A pivotal part of this research involved a scientific technique called mass spectrometry, which is relatively new to the science of biology. The ultra-precise mass spectrometry experiments were done by HMS professor of cell biology Steven Gygi. Mass spectrometry is used to measure the exact weight (the mass) and thus identify each individual protein in a sample. It is a technique originally devised by physicists for analyzing atomic particles. But in recent years [mass spectrometry](#) was adapted and refined for new and powerful uses in basic biological research. Other studies using similar techniques to date have focussed on small groups of related

proteins or single celled model organisms such as bacteria and yeast.

Despite the huge amount already known about the fruit fly and its genetic endowment, much about the function of thousands of proteins remains a mystery. This map, however, now gives us precise clues about their function. Filling in the detailed protein map can help scientists gain important insights into the process of development, that is, how a creature is put together, maintained and operated.

"Our analyses also sheds light on how proteins and protein networks have evolved in different animals," said K. G. Guruharsha, a postdoctoral fellow in Artavanis-Tsakonas's lab and a first author on the paper.

Co-lead authors on the paper included Jean-Francois Rual, also a postdoctoral fellow in Artavanis-Tsakonas's lab, and Julian Mintseris and Bo Zhai, both research fellows in Gygi's lab.

Also important in this effort was the work of K. VijayRaghavan, at the National Centre for Biological Sciences in Bangalore, India. Similarly, crucial contributions to this work also came from the University of California, in Berkeley, where Susan E. Celniker collaborated through her studies in the fruit fly genome center.

More information: "A Protein Complex Network of *Drosophila melanogaster*" Guruharsha et al. *Cell*, 28 October, 2011 Volume 147, Issue 3

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