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WEIZMANN INSTITUTE OF SCIENCE
Science Tips

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Switching Goals

A computer simulation shows how evolution may have speeded up

Is heading straight for a goal the quickest way there? If the name of the game is evolution, suggests new research at the Weizmann Institute of Science, the pace might speed up if the goals themselves change continuously.

Nadav Kashtan, Elad Noor and Prof. Uri Alon of the Institute's Molecular Cell Biology and Physics of Complex Systems Departments create computer simulations that mimic natural evolution, allowing them to investigate processes that, in nature, take place over millions of years. In these simulations, a population of digital genomes evolves over time towards a given goal: to maximize fitness under certain conditions. Like living organisms, genomes that are better adapted to their environment may survive to the next generation or reproduce more prolifically. But such computer simulations, though sophisticated, don't yet have all the answers. Achieving even simple goals may take thousands of generations, raising the question of whether the three-or-so billion years since life first appeared on the planet is long enough to evolve the diversity and complexity that exist today,

Evolution takes place under changing environmental conditions, forcing organisms to continually readapt. Intuitively, this would slow things down even further, as successive generations must switch tack again and again in the struggle to survive. But when Kashtan, Noor and Alon created a simulation in which the goals changed repeatedly, they found that its evolution actually speeded up. They even found that the more complex the goal – i.e., the more generations needed reach it under fixed conditions – the faster evolution accelerated in response to changes in that goal.

Computerized evolution ran fastest, the scientists found, when the changes followed a pattern they believe may be pervasive in nature. In previous research, Kashtan and Alon had shown that evolution may often be modular – involving adjustments to standard parts, rather than wholesale remodeling. They theorized that the forces acting on evolution may be modular as well, and for each goal, they defined subgoals that could each change in relation to the others. "In an organism, for example, you might classify these subgoals as the need to eat, the need to keep from being eaten, and the need to reproduce. The same subgoals must be fulfilled in each new environment, but there are differences in nuance and combination," says Kashtan. "We saw a large speedup, for instance, when we repeatedly exchanged an "OR" for an "AND" in the computer code defining our goals, thus changing the relationship between subgoals."

Although the main aim of this research, which appeared recently in the *Proceedings of the National Academy of Sciences* (PNAS), was to shed light on theoretical questions of evolution, it may have some practical implications, particularly in engineering fields in which evolutionary tools are commonly used for systems design; and in computer science, by providing a possible way to accelerate optimization algorithms. ❙

Prof. Uri Alon's research is supported by the Nella and Leon Benoziyo Center for Neurological Diseases; the Clore Center for Biological Physics; the Yad Abraham Research Center for Cancer Diagnostics and Therapy; the Leon and Gina Fromer Philanthropic Fund; the Kahn Family Foundation for Humanitarian Support; Keren Isra-Pa'amei Tikva Ltd.; the Minerva Stiftung Gesellschaft fuer die Forschung m.b.H.; the James and Ilene Nathan Charitable Directed Fund; the Harry M. Ringel Memorial Foundation; the estate of Ernst and Anni Deutsch, Liechtenstein; and Mr. and Mrs. Mordechai Segal, Israel.

Shrinking Giants, Exploding Dwarves

When white dwarf stars explode, they leave behind a rapidly expanding cloud of "stardust" known as a Type Ia supernova. These exploding events, which shine billions of times brighter than our sun, are all presumed to be extremely similar, and thus have been used extensively as cosmological reference beacons to trace distance and the evolution of the Universe.

Astronomers have now – for the first time ever – provided a unique set of observations obtained with the ESO Very Large Telescope in Chile and the 10-meter Keck telescope in Hawaii, enabling them to find traces of the material that had surrounded a white dwarf star before it exploded. Their data set is unique in that no Type Ia supernova event has ever been observed at this level of detail over a several-month period following the explosion.

These observations support a widely accepted model proposing that a white dwarf star interacts with a companion star – a red giant. Due to the white dwarf's strong gravitational pull, this companion star continuously loses mass through 'force feeding' its gases to the white dwarf. When the mass of the white dwarf grows past a critical value, it explodes.

Through their observations, which took place over the course of four months, and combined with archival data, the astronomers detected the presence of a number of expanding shells surrounding a Type Ia supernova event. The make-up of these shells suggests they are the remnants of the red giant star that fed the white dwarf.

These results were recently published in the journal *Science*. The data were collected by two teams of researchers; one at ESO headed by Dr. Ferdinando Patat, and one at the California Institute of Technology, USA, led by Dr. Avishay Gal-Yam. Dr. Gal-Yam has recently joined the Weizmann Institute of Science as a senior scientist in the Condensed Matter Physics Department. ❙

A Gene for Metastasis

Weizmann Institute Scientists reveal the actions of a key player in colorectal cancer

Colorectal cancer is one of the most prevalent cancers in the Western world. The tumor starts off as a polyp but then turns into an invasive and violent cancer, which often spreads to the liver. In an article recently published in the journal *Cancer Research*, Prof. Avri Ben-Ze'ev and Dr. Nancy Gavert of the Weizmann Institute's Molecular Cell Biology Department reveal mechanisms that help this cancer metastasize.

In a majority of cases, colorectal cancer is initiated by changes in a key protein – beta-catenin. One of the roles of this protein is to enter the cell nucleus and activate gene expression. But in colorectal and other cancers, beta-catenin over-accumulates in the cell and inappropriately activates genes, leading to cancer.

Surprisingly, one of the genes activated by beta-catenin, which had been previously detected in colorectal cancer cells by Ben-Ze'ev's group, codes for a receptor called L1-CAM. This receptor is a protein usually found on nerve cells, where it plays a role in nerve cell recognition and motility. What is this receptor doing in cancer cells? Ben-Ze'ev's previous research had shown that L1-CAM is only expressed on certain cells located at the invasive front of the tumor tissue, hinting that it could be an important player in metastasis.

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In this study, the scientists found that colorectal cancer cells engineered to express the L1-CAM gene indeed spread to the liver, while those cells lacking L1-CAM did not.

In collaboration with Prof. Eytan Domany and research student Michal Sheffer of the Insitute's Physics of Complex Systems Department, Ben-Ze'ev then compared the expression of genes induced by L1-CAM in cultured colon cancer cells to those in 170 samples of colorectal cancer tissue removed from patients, and in 40 samples of normal colon tissue. Out of some 160 genes induced by L1-CAM, about 60 were highly expressed in the cancerous tissue, but not in normal colon tissue. Ben-Ze'ev plans to conduct further research into the role of these genes, to uncover L1-CAM's function in metastasis. ❙

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