Slow motion waves of jumping genes in the human genome

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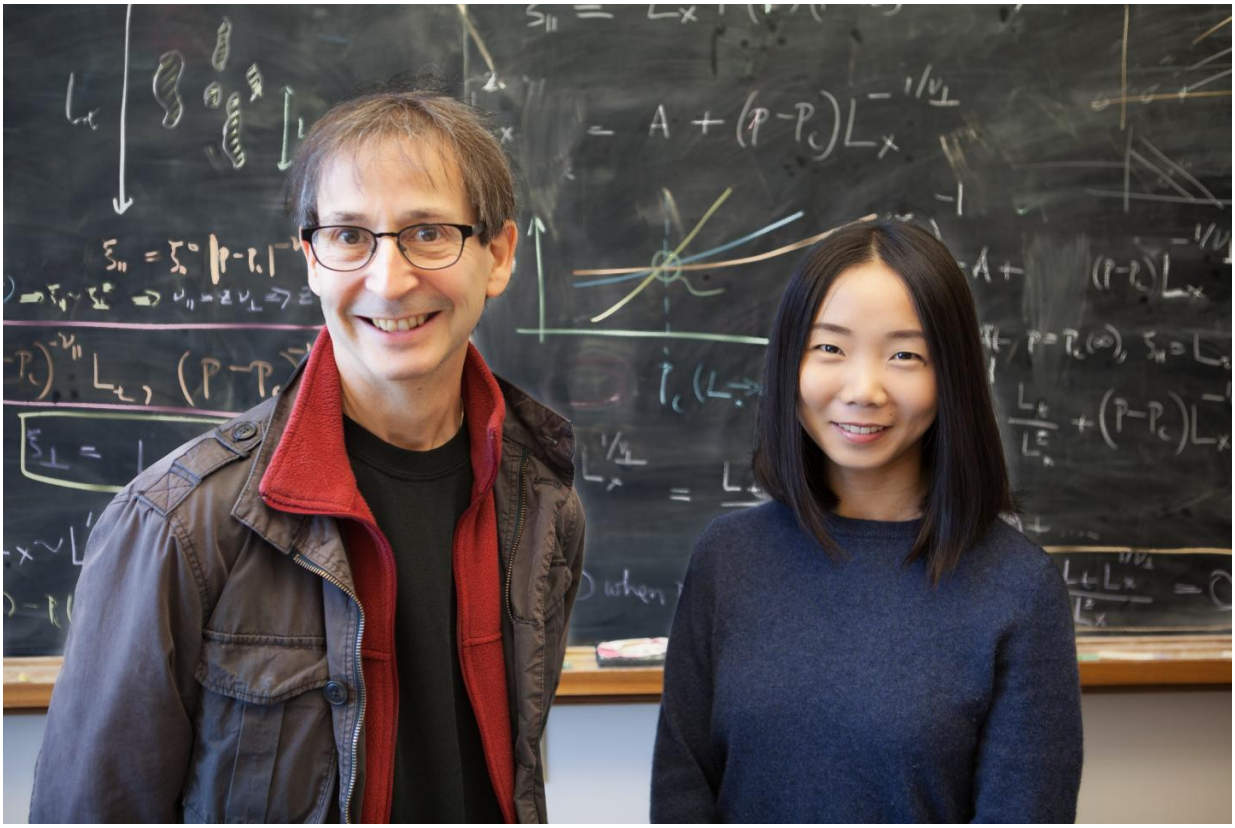

Physicists Nigel Goldenfeld (left) and Chi Xue, at the Carl R. Woese Institute for Genomic Biology at the University of Illinois at Urbana-Champaign. Credit: Kathryn Faith.

Nature is full of parasites—organisms that flourish and proliferate at the

expense of another species. Surprisingly, these same competing roles of parasite and host can be found in the microscopic molecular world of the cell. A new study by two Illinois researchers has demonstrated that dynamic elements within the human genome interact with each other in a way that strongly resembles the patterns seen in populations of predators and prey.

The findings, published in *Physical Review Letters* by physicists Chi Xue and Nigel Goldenfeld, are an important step toward understanding the complex ways that genomes change over the lifetime of individual organisms, and how they evolve over generations.

"These are genes that are active and are doing genome editing in real time in living cells, and this is a start of trying to really understand them in much more detail than has been done before," said Goldenfeld, who leads the Biocomplexity research theme at the Carl R. Woese Institute for Universal Biology (IGB). "This is helping us understand the evolution of complexity and the evolution of genomes."

The study was supported by Center for the Physics of Living Cells, a Physics Frontiers Center at Illinois supported by the National Science Foundation, and the NASA Astrobiology Institute for Universal Biology at Illinois, which Goldenfeld directs.

Goldenfeld and Xue embarked on this work because of their interest in transposons, small regions of DNA that can move themselves from one part of the genome to another during the lifetime of a cell—a capability that has earned them the name "jumping genes." Collectively, various types of transposons make up almost half of the human genome. When they move around, they may create mutations in or alter the activity of a functional gene; transposons can therefore create new genetic profiles in a population for natural selection to act on, in either a positive or negative way.

The Illinois researchers wanted to learn more about how evolution works on this level, the level of whole organisms, by looking at the metaphorical ecosystem of the human genome. In this view, the physical structure of the DNA that makes up the genome acts like an environment, in which two types of transposons, long interspersed nuclear elements (LINEs) and short interspersed nuclear elements (SINEs), have a competitive relationship with one another. In order to replicate, SINEs steal the molecular machinery that LINEs use to copy themselves, somewhat like a cuckoo bird tricks other birds into raising her chicks for her while abandoning their own.

With help from Oleg Simakov, a researcher at the Okinawa Institute of Science and Technology, Xue and Goldenfeld focused on the biology of L1 elements and Alu elements, respectively common types of LINEs and SINEs in the human genome.

The researchers adopted methods from modern statistical physics and modeled the interaction between Alu and L1 elements mathematically as a stochastic process—a process created from chance interactions. This method has been successfully applied in ecology to describe predator-prey interactions; Xue and Goldenfeld simulated the movements of transposons within the human genome with the same mathematical method. Their models included a detailed accounting for how Alu elements steal the molecular machinery L1 elements use to copy themselves.

Xue and Goldenfeld's results predicted that populations of LINE and SINE elements in the genome are expected to oscillate the way those of, for example, wolves and rabbits might.

"We realized that the transposons' interaction actually was pretty much like the predator-prey interaction in ecology," said Xue. "We came up with the idea, why don't we apply the same idea of predator-prey

dynamics . . .we expected to see the oscillations we see in the predator-prey model. So we first did the simulation and we saw the oscillations we expected, and we got really excited."

In other words, too many SINEs and the LINEs start to suffer, and soon there are not enough for all the SINEs to exploit. SINEs start to suffer, and the LINEs make a come-back. Xue and Goldenfeld's model made the surprising prediction that these oscillations occur over a timescale that is longer than the human lifespan—waves of Alu elements and L1 elements pushing and pulling at each other in slow motion across generations of the human genomes that carry them.

"The most enlightening aspect of the study for me was the fact that we could really compute the timescales, and see that it is possible that we could observe these things," said Goldenfeld. "We have a prediction for what happens in single cells, and we may be able to actually do an experiment to observe these things, though the period is longer than the lifetime of a single cell."

In a related study, Goldenfeld's laboratory has collaborated with the laboratory of fellow physicist and IGB Biocomplexity research theme member Thomas Kuhlman to visualize the movements of transposons within the genomes of living cells. Using this type of innovative technology, and by studying the history of molecular evolution in other species, Goldenfeld and Xue hope to test some of the predictions made by their model and continue to gain insight into the dynamic world of the genome.

More information: Chi Xue et al, Stochastic Predator-Prey Dynamics of Transposons in the Human Genome, *Physical Review Letters* (2016). DOI: 10.1103/PhysRevLett.117.208101