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Study of human migration could help understand cancer metastasis

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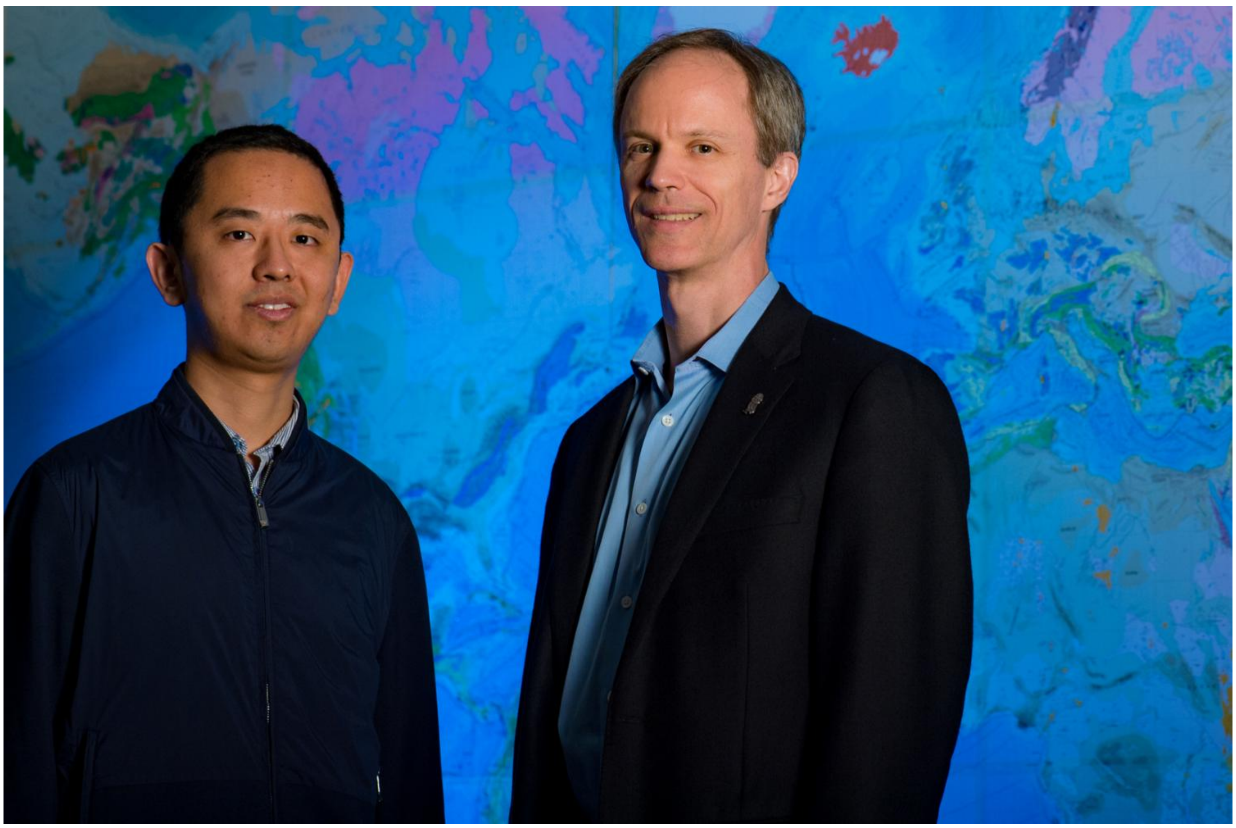

A computer model of human migration in the Americas by Rice University researchers Dong Wang (left) and Michael Deem could also shed light on the behavior of metastatic cancers. Credit: Jeff Fitlow/Rice University

What could cancer cells and drug-resistant bacteria possibly have in common with Stone Age settlers of the Americas? They're all migratory, and at one time or other, each finds the going a bit easier in a specific direction.

For cancer cells, the path of least resistance is often along tissue boundaries rather than through them, and studies have found that bacteria can become drug-resistant more quickly in nonhomogenous environments. In the case of humans settling America, a new study from Rice University finds that migration was easier moving east-west as opposed to north-south, largely because the knowledge needed to live in the same climate zones was easily transferable.

The research is available online in the *Journal of the Royal Society Interface*.

Lead researcher Michael Deem said he conceived the study while reading Jared Diamond's "Guns, Germs and Steel," a 1998 Pulitzer Prize-winning book that argued that differences in power and technology between human societies stem more from environmental and geographic factors than from intellectual, genetic or cultural attributes.

"One hypothesis he put forward was that migration was more rapid in the east-west direction than in the north-south direction because the crops and animals people relied upon tended to remain the same if the people migrated east-west within climate zones and tended to change if they moved north-south between climate zones," said Deem, Rice's John W. Cox Professor in Biochemical and Genetic Engineering and a senior scientist at Rice's Center for Theoretical Biological Physics.

"The idea is that it takes extra time and effort to develop the techniques and knowledge necessary to survive in a new climate, and that creates more of an obstacle to north-south migration. I thought that was really interesting, and I always wanted to do something a little more quantitative on that problem," he said.

Deem, who chairs Rice's Department of Bioengineering and is a professor of physics and astronomy, specializes in using statistical mechanics to design computer simulations that accurately capture the complexity of nature. His work has led to mathematical laws of biology and includes computer models that predict how well next year's flu vaccine will work, how globalization affects the world economy and how the speed of biological evolution increases with time because of evolution.

A common theme throughout Deem's research is "modularity," a feature of data that can be revealed through various techniques. For migrating bacteria, a specific gene could be a module of information, and an analogous module for the first humans in America would be specific knowledge about local environments or effective techniques for farming or raising animals.

"A big aspect that we're interested in is how modularity accelerates the adaptation of biological systems, and more specifically in this case, how the modularity of knowledge interacts with asymmetry during migration," Deem said. "What we learn can be broadly applied, because the physical dynamics are similar in the case of the east-west verses north-south migration of people in the Americas and in the case of bacteria migrating in a Petri dish where there's a right-left versus up-down antibiotic gradient. One could also envision analogous scenarios with invasive species or metastatic cancer."

In designing the model of human migration in the Americas, Deem and graduate student Dong Wang incorporated variables related to environment, the timing and speed of migration, knowledge creation and communication, genetics and the overall "fitness" or health of populations. The model predicts how populations expand across a 9-by-25 grid that simulates the length and approximate width of the Americas.

Archaeological evidence shows that the first Americans arrived from Asia via a land bridge across the present-day Bering Strait during a glacial ice age about 20,000 years ago. In keeping with the dominant theory among archeologists, Deem and Wang's model begins with humans entering the Americas from the far north.

"Once a population reaches the carrying capacity on their site, and the fitness is above a threshold, they will attempt to migrate to a new site," Wang said. "What we will see is that there is a front of migration, an east-west line that moves south over time."

The likelihood of migration into an adjacent site depends partly on how similar the environment is, and the environment in the east-west direction changes less, on average, than it does north-south.

"The more modular knowledge is, the easier it is to optimize, and the easier it is to transmit that information to other individuals and the easier it is to pioneer new sites," Deem said. "If tasks are interdependent—perhaps the corpus of knowledge required to grow a particular crop also interacts with knowledge about how to make tools or when the seasons change—the easier it is to pioneer new sites. The more things interact, the more difficult it is to optimize that problem, and that's a situation with less modularity of knowledge."

Wang said the model was confirmed with empirical data where possible.

"The model includes genetics, and we can examine the genes of individuals," he said. "That allows us to look at the genetic distance between different populations at different places and times, and when we compare those actual measures from the archeological record, we find that they match pretty well. Another empirical check is the actual rates of migration and the asymmetry of the rates of migration in the archeological record."

Deem said the model is the first to both explicitly quantify the effect of modularity on fitness and examine how environmental asymmetry affects human migration.

"We learned that Jared Diamond's idea makes sense," Deem said. "It is the case that when the asymmetry in the north-south direction of the environments is larger than in the east-west direction, then it is harder to migrate in the north-south direction."

He and Wang will next focus on modifying the model to focus specifically on cancer metastasis.

"In solid tumor cancers, for example, there's an asymmetry in the radial direction, away from the tumor versus on the surface of the tumor," Deem said. "There also is an asymmetry as the cells metastasize and go through different tissues in the body. So, there's an asymmetry along membranes versus through membranes, and there are recent empirical studies that provide new data that we can use to help examine the effect of these asymmetries in greater detail."

More information: Dong Wang et al. Modular knowledge systems accelerate human migration in asymmetric random environments, *Journal of The Royal Society Interface* (2016). DOI: 10.1098/rsif.2016.0778

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