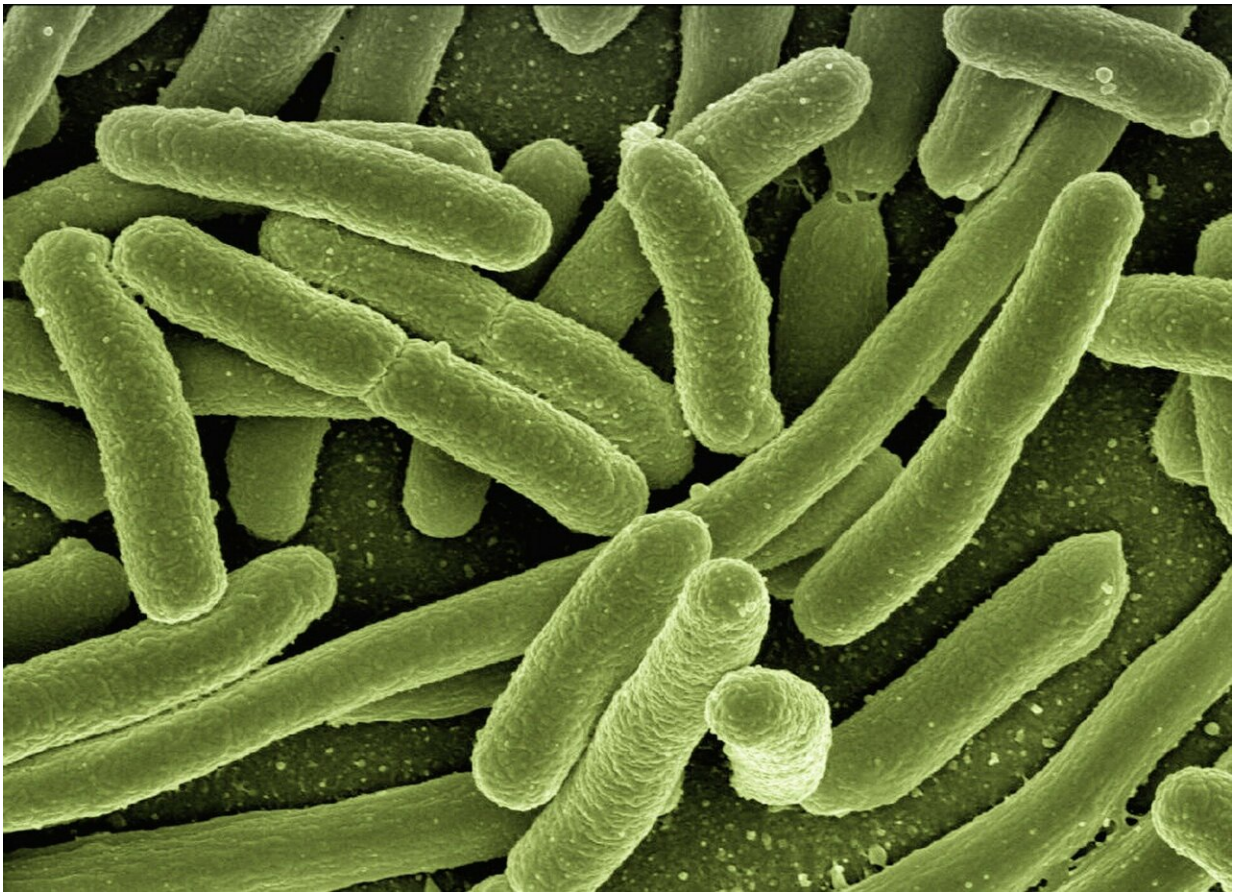


Math reveals how diseases progress and bacteria develop drug resistance

November 21 2019, by Hayley Dunning



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Scientists from Imperial and the University of Bergen have found a new way to predict how a disease will likely progress in individual patients.

This could help patients receive more targeted treatments earlier in the progress of their disease.

How the same disease progresses in different patients often varies widely. Understanding this variability is important for precision medicine, where detailed knowledge of individual patients is used to design the best targeted treatments.

However, learning the varied pathways of diseases and using them to predict future outcomes is challenging. Human researchers cannot hope to remember or analyze enough examples of patient data to provide the most reliable picture.

In the new study, the team used an algorithm called HyperTraPS, which uses biomedical data from many patients—hundreds, or thousands of individuals—to build a road map of the different pathways that a disease takes over time.

Different disease branches

Dr. Iain Johnston from the University of Bergen in Norway, who led the project, said: "Picture a river that branches out into a wide delta. Patients start out healthy—upstream in the river—and different patients go down different branches as the disease progresses and they acquire more symptoms.

"HyperTraPS learns the structure of the river delta from data, and predicts which river branches are more or less likely—and, importantly, where you'll end up if you're currently at a particular point."

By learning these branching patterns of disease progression, HyperTraPS has helped provide a refined risk assessment for malaria, based on data from thousands of Gambian children. The approach also revealed

diverse pathways of ovarian cancer progression, where the first mutation to occur appears to play a large role in determining subsequent mutations.

Using big data to answer biomedical questions

Co-author Dr. Sam Greenbury, now with the ITMAT Data Science group at Imperial, said: "Our approach especially shines in its generalizability. HyperTraPS can learn about the behavior of any system where the presence or absence of features can be observed.

"This is very useful for tracking [disease](#) markers, learning about biological evolution and other processes that occur over time. We can use the vast and growing quantities of [big data](#) to generate new insights into a whole host of biomedical questions."

The team used this generalizability to explore another medically important question—how tuberculosis evolves to become resistant to antibiotics.

Tuberculosis acquires resistance through mutations, and HyperTraPS has revealed the patterns of these mutations in TB bacteria reported from a group of 1000 Russian patients. These patterns help predict which mutation a bacterium will acquire next, and hence which drugs may be more effective for a given case.

Progressive diseases, aging and evolution

HyperTraPS was developed with funding from the EPSRC Centre for the Mathematics of Precision Healthcare (CMPH) in the Department of Mathematics at Imperial, and the Alan Turing Institute.

Professor Mauricio Barahona, co-author of the research and director of CMPH from the Department of Mathematics at Imperial, said: "This is an example of how mathematics can help us solve seemingly different problems by viewing them under a common prism. We are commonly faced with situations where we have a snapshot of a population of individuals, each at a different stage of a process.

"Our method allows us to establish the likely paths leading to our observation. This approach has applications not only to progressive diseases and the emergence of antibiotic resistance but more broadly to other processes where features are acquired sequentially."

The team are now using HyperTraPS to learn about other progressive diseases, aging, and evolution, and even to analyze how students complete tasks in online courses.

More information: Sam F. Greenbury et al. Inferring high-dimensional pathways of trait acquisition in evolution and disease, *Cell Systems* (2018). DOI: [10.1101/409656](https://doi.org/10.1016/j.celsys.2018.08.005)

Provided by Imperial College London

Citation: Math reveals how diseases progress and bacteria develop drug resistance (2019, November 21) retrieved 4 May 2024 from <https://phys.org/news/2019-11-math-reveals-diseases-bacteria-drug.html>

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