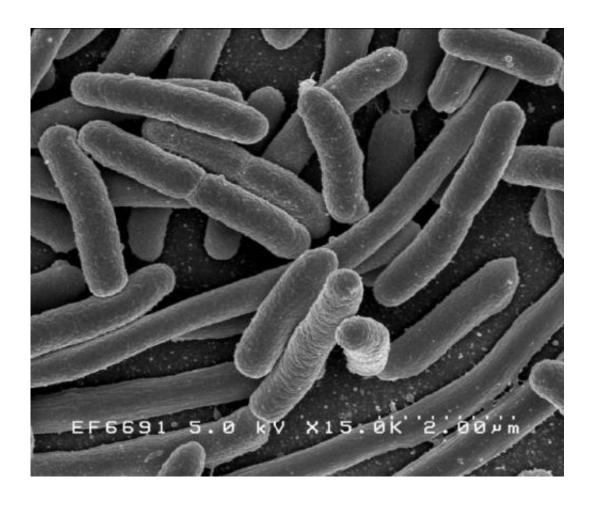


How bacteria adapt their machinery for optimum growth

October 16 2020



Escherichia coli. Credit: Rocky Mountain Laboratories, NIAID, NIH

The most important components for the functioning of a biological cell are its proteins. As a result, protein production is arguably the most important process for cell growth. The faster the bacterial growth rate,



the faster protein synthesis needs to take place. Because protein synthesis is the most expensive cellular process in terms of cellular resources usage, it appears reasonable to assume that the cell to increases production capacities by hosting more copies of the complicated machinery in proportion to its growth rate. This would mean that in order for growth to double, twice as many copies of all components of the translation machinery would be needed.

It has been clear since the 1960s, however, that it's not that simple. Instead, the composition of the 'cocktail' of individual components in the machinery, which itself is made from proteins and RNA, varies with the growth rate. A new, complex computer model developed in Düsseldorf shows what concentrations of the individual components are needed in order to produce different synthesis rates, explaining for the first time the reasons behind the observed variations across growth conditions.

Xiao-Pan Hu, a doctoral student in Prof. Dr. Martin Lercher's Computational Cell Biology group at the HHU, developed the model. Hu used computer modeling to encode established biochemical principles at the cellular level. The resulting model can be used to calculate the speed with which a cell can produce its components and thus predicts <u>cell</u> <u>growth</u> based on a predefined composition of its machinery.

Theoretically, each production rate can be realized using a large number of different molecule concentrations. The question is: What does nature do? Which one of the many feasible compositions do real Escherichia coli ('E. coli') bacteria use and why? Hu and his colleagues have based their work on a simple assumption reflected everywhere in nature: an organism generally has an evolutionary advantage if it needs as few resources as possible for its development. Consequently, the team searched through the many possible compositions for the one that is 'cheapest' for the cell, i.e., the one that requires the smallest possible total mass of molecules.



Comparisons with experimental data show that this assumption is correct and accurately predicts the concentrations measured in real E. coli bacteria colonies. This allowed the Düsseldorf-based research team not only to describe the data quantitatively but also to actually understand the reasons behind the data, namely that a principle found in many other areas of life also applies here.

In further analyses, the <u>model</u> also proved accurate for situations where the bacteria are exposed to antibiotics. In exceptional circumstances like these, the bacteria are particularly stressed and need a toolset that is arranged differently in order to grow.

The research group is currently investigating whether the findings for <u>protein</u> synthesis can also be applied to other cellular processes and other organisms. The models developed as part of this work should also help to design biotech procedures more efficiently. They make it possible to calculate the optimum concentrations of the individual components in the cell for the desired biological production.

More information: Xiao-Pan Hu et al. The protein translation machinery is expressed for maximal efficiency in Escherichia coli, *Nature Communications* (2020). DOI: 10.1038/s41467-020-18948-x

Provided by Heinrich-Heine University Duesseldorf

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