Fundamental limitations to the rate of bacterial cell division

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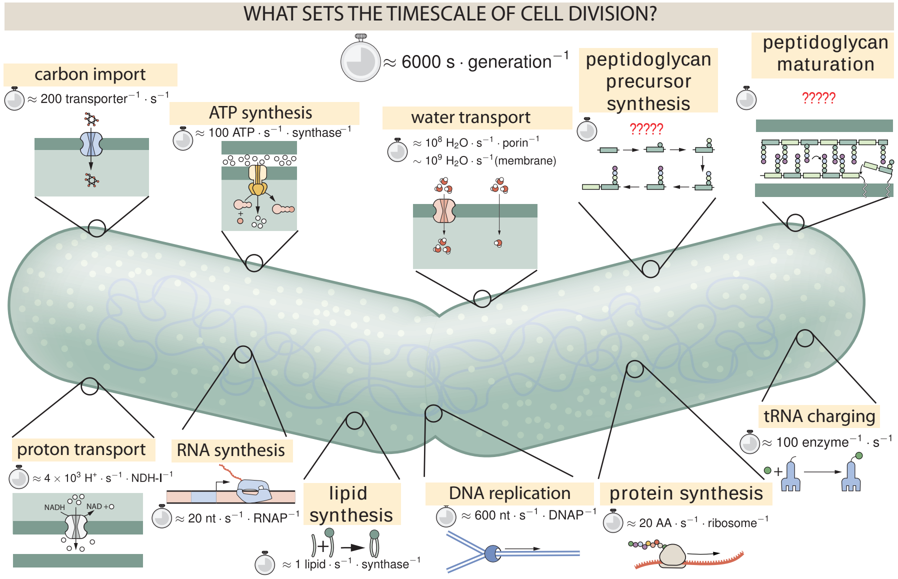

Figure 1: **Transport and synthesis processes necessary for cell division.**

1 Introduction

The intimate relationship between the environment and cellular growth rate has remained a major topic of inquiry in bacterial physiology for over a century.

Points to emphasize

- The past decade of work in proteomics has made high-througput absolute measurement of protein abundance a reality. Recent groups have used mass spectrometry and ribosomal profiling to quantify growth-dependent effects on protein copy numbers across growth conditions. In this work, we assemble four recent datasets that examine how cellular proteome is influenced by the total growth rate.

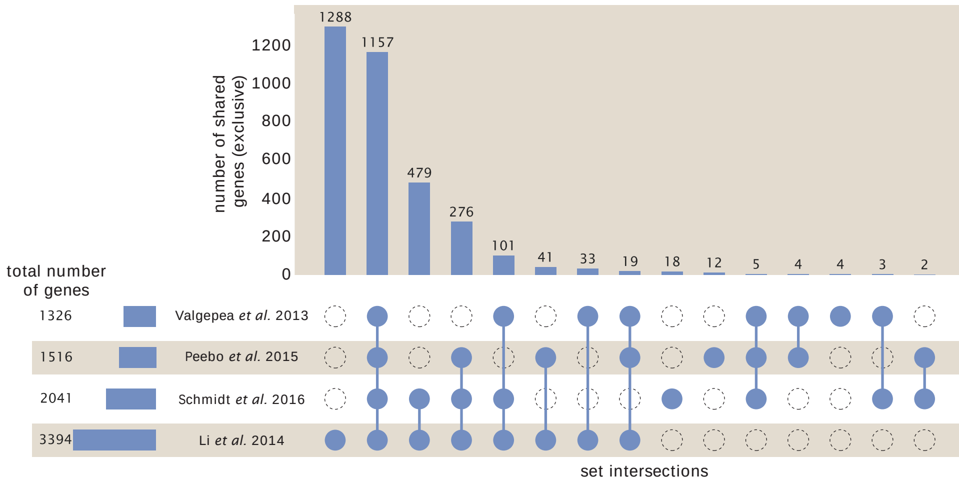

Figure 2: **Summary of the compiled datasets.**

2 A comprehensive examination of the *E. coli* proteome

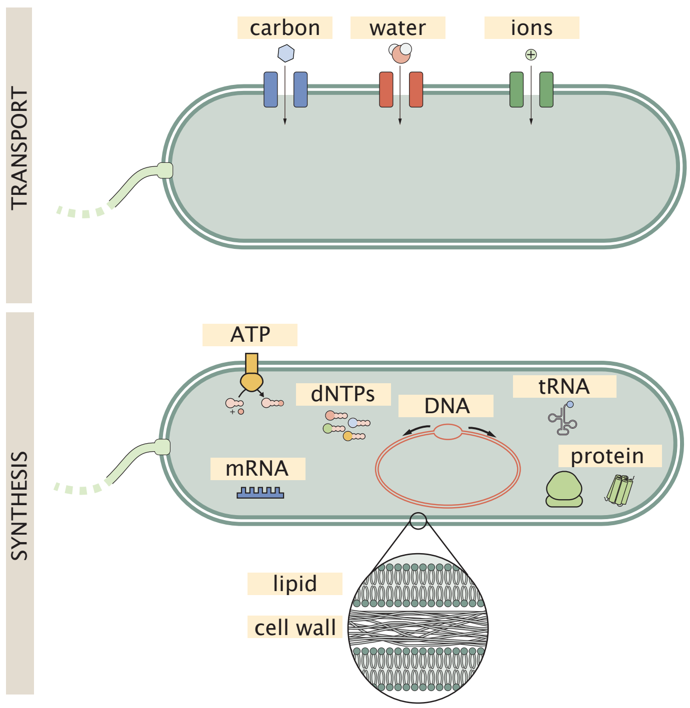

Figure 3: **Potential bottlenecks for bacterial growth.** The growth rate of *Escherichia coli* may be limited by the transport of biochemical precursors across the cell membrane (top panel) or by the synthesis of various molecules and macromolecules. Illustrative examples of the potential bottlenecks are provided in both panels.

3 Transport of Biochemical Building Blocks

We begin with an interrogation of some of the myriad transport systems bacteria use to bring extracellular materials (such as carbon, water, and ions) into the cell.

3.1 Carbon Transport

All macromolecules synthesized by cells include carbon as the primary elemental constituent. It is therefore reasonable to consider the acquisition of carbon from the environment, typically in the form of sugar, as a candidate process which sets the bacterial speed limit. We can a combination of biological intuition and the vast literature on the molecular composition of *E. coli* to make an order-of-magnitude estimate for the total number of sugar transporters needed double.

For convenience, we will consider a condition in which glucose is the primary carbon source in a growth medium. In standard laboratory conditions, a minimal medium supplemented with only glucose will have a growth rate of $\approx 1\text{generation}\cdot\text{hr}^{-1}$ which is an approximate doubling time of ≈ 3000 seconds. During this time, the cell must be able to import enough carbon molecules to double all macromolecules.

We can begin by using the well justified estimate that the typical *E. coli* cell is $\approx 70\%$ water by mass, yielding a $\approx 30\%$ dry mass (BNID: 109049, [1]). Exponential growth of *E. coli* in a glucose based medium results in an average cell volume of 1 fL, bringing our total dry mass to 30 pg. Assuming half of this dry mass is protein (0.15 pg), we can estimate how many carbons are present in the protein pool.

Let's assume that a standard protein is approximately 300 amino acids long, which comes out a mass of ≈ 30 kDa. From this, we estimate that the total number of amino acids (incorporated into protein) is

$$N_{\text{AA}} = \left(1.5\times10^{-13}\,\text{g}\right)\times\left(\frac{1\,\text{protein}}{3\times10^{4}\,\text{Da}}\right)\times\left(\frac{6\times10^{23}\,\text{Da}}{1\,\text{g}}\right)\times\left(\frac{3\times10^{2}\,\text{AA}}{\text{protein}}\right)\approx 2.5\times10^{8}\,\text{Amino Acids.} \tag{1}$$

The typical amino acid consists of a two-carbon backbone with a ≈ 3 carbon side-chain. Thus, assuming the typical amino acid contains ≈ 5 carbons, the total mass of carbon in the protein pool can be calculated as

$$N_{\text{C}}^{(\text{protein})} = N_{\text{AA}}\times\frac{\text{C}}{\text{AA}} = 2.5\times10^{8}\,\text{AA}\times\frac{5\,\text{C}}{\text{AA}}\approx 5\times10^{9}\,\frac{\text{C}}{\text{cell}}. \tag{2}$$

Since we approximated that about half of the dry mass is protein, it's reasonable to assume that the remaining half of the dry mass has a similar composition, permitting us to say that

$$N_{\text{C}}^{(\text{cell})}\approx 2\times N_{\text{C}}^{(\text{protein})} = 10^{10}\,\frac{\text{C}}{\text{cell}}. \tag{3}$$

With a handle on the total number of carbons needed per cell, we can now try to estimate how many sugar transporters would be needed to transport 100 billion carbon atoms per standard cell doubling time of ≈ 3000 seconds. With 6 carbon atoms per glucose molecule, we can estimate the minimum glucose flux across the membrane to be

$$J_{\text{glucose}} = \frac{10^{10}\,\text{C}}{\text{cell}}\times\frac{1\,\text{glucose}}{6\,\text{C}}\times\frac{1\,\text{cell}}{3\times10^{3}\,\text{s}}\approx 5\times10^{6}\,\frac{\text{glucose}}{\text{s}}. \tag{4}$$

The chief glucose transport system of *E. coli* (the PTS system) can transport $\approx 200\,\text{glucose}\cdot\text{s}^{-1}$ (BNID: 103693 [1]) meaning that the *minimum* number of glucose transporters per cell needed to double the cellular carbon content is

$$N_{\text{tpr.}}\approx\frac{J_{\text{glucose}}}{J_{\text{transporter}}} = \frac{5\times10^{6}\text{glucose / s}}{2\times10^{2}\,\text{glucose / s}}\approx 2\times10^{4}\,\text{tpr. / cell.} \tag{5}$$

3.2 Water Transport

References

[1] Ron Milo, Paul Jorgensen, Uri Moran, Griffin Weber, and Michael Springer. BioNumbers—the database of key numbers in molecular and cell biology. *Nucleic Acids Research*, 38(suppl_1):D750–D753, January 2010.