

Control of cell volume in rod-shaped bacteria

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Bacteria exhibit a high degree of intracellular macromolecular crowding. To control the level of crowding cells must increase their volumes in response to the accumulation of biomass during growth. However, to date it is not understood how cells achieve this task. Using *Escherichia coli* as a model bacterium we found that cell-to-cell variations in dry-mass density, a read-out of intracellular crowding, can be smaller than 3%. At the same time we found that dry-mass density shows systematic variations as a function of cell dimension in constant metabolic environments or during changes of growth conditions, while the ratio between cell-surface area and dry mass remained constant. We thus concluded that crowding homeostasis is achieved indirectly by coupling the rate of cell-surface expansion directly to the rate of dry-mass growth. Large differences in surface-to-volume ratios observed between different growth media would therefore naturally lead to large variations of mass density. However, we found these to be compensated by inverse changes of the surface-to-mass ratios, thus reducing variations of mass density between growth conditions. Through a range of perturbations and the analysis of single-cell correlations we then elucidate potential mechanisms underlying surface-to-mass coupling and adaptation. Together, our experiments reveal important regulatory relationships underlying crowding and envelope homeostasis.