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Macromolecular crowding: a foreword

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As far as my coworkers and I have been able to determine, proteins and nucleic acids constitute at least 20–30% of the total mass (and volume) of all living organisms, without exception. Although the local composition varies highly from point to point within an individual cell, nevertheless it seems that no intracellular compartment contains a significantly smaller volume fraction of macromolecules, and some compartments, such as the mitochondrial inner matrix, contain significantly higher volume fractions. Evidently, much of the chemistry of life — as opposed to laboratory biochemistry — takes place within a medium that we shall term 'crowded', i.e., containing a substantial volume fraction of macromolecules (Fig. 1). Specifically, the term 'crowding' is meant to connote the cumulative influence of large concentrations of macromolecules upon the behavior of one or more dilute test species of molecules with which the space-filling macromolecules interact only in a nonspecific fashion, i.e., by steric repulsion or weak electrostatic or hydrophobic interaction. It is our thesis that in order to bridge the gap between laboratory biochemistry and the chemistry of living organisms, it is necessary to investigate whether and to what extent crowding influences the rates and equilibria of different types of biochemical reactions. This is the motivation for much of the work presented in this special issue.

During the last forty years it has gradually become recognized by physical chemists that individual macromolecular species in crowded media exhibit both dynamic and equilibrium properties, including chemical reactivity, that may be qualitatively different from the those of the same species in a dilute or uncrowded medium (see Ref. [1] for a recent review). We are privileged to present in this special issue retrospective contributions from A.G. Ogston and T.C. Laurent, who individually and jointly pioneered the physico-chemical study of the behavior of proteins in concentrated solutions of biopolymers, and discovered many of the basic principles elaborated by succeeding investigators.

The remaining papers treat a variety of topics, but all of them concern themselves in one way or another with the effect of high total concentrations of 'inert' macromolecules or small molecule solutes upon the dynamic or equilibrium behavior of one or more species of macromolecule in a fluid medium. Aside from the relevance of such studies to an understanding of cell biology, crowded media are of interest because in many cases, the equilibrium and time-dependent behavior of such media cannot be deduced even qualitatively from the observed behavior of their individual components at limiting low concentrations. It is indeed a fascinating and biologically important case of the whole being considerably greater than the sum of the parts.

References

[1] S.B. Zimmerman and A.P. Minton, Ann. Rev. Biophys. Biomol. Struct., 22 (1993) 27.

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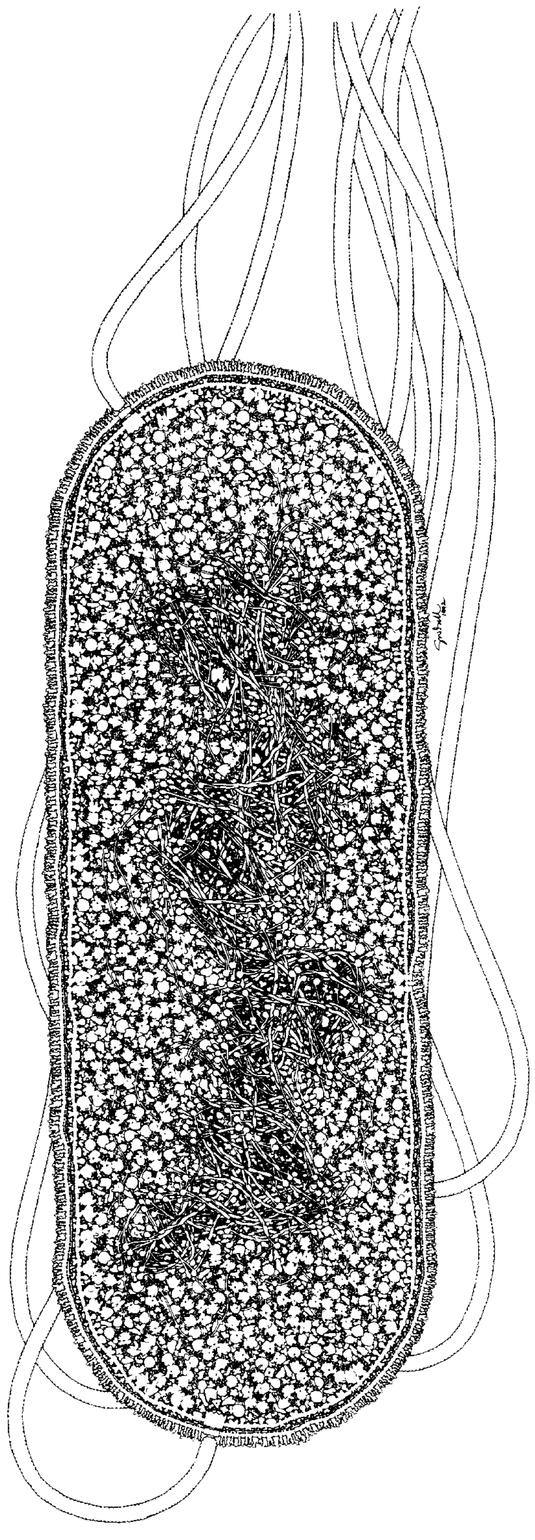

Fig. 1. Cartoon of the *E. coli* cell at 180000× magnification. Various macromolecular species and complexes are drawn to scale with number densities estimated from literature sources. Reproduced with permission from "The Machinery of Life" by David S. Goodsell, Springer Verlag, New York, 1992.