Diffusion coefficient as a function of mass for globular macromolecules

Michael J. Saxton[1]*

[1]Dept of Biochemistry & Molecular Medicine, Univ of California, Davis, California, USA

*mjsaxton@ucdavis.edu

How well can the diffusion coefficient *D* of a globular biomolecule be predicted from its molecular mass *MW*?

Diffusion measurements in heterogeneous systems can be improved by the use of scalable tracers, in which the size is varied alone at constant shape, surface properties, diffusion mechanism, deformability, and other properties affecting diffusion [1]. Before trying to design a *de novo* series of scalable globular proteins, it is appropriate to examine how scalable the commonly used *de antiquo* globular proteins are.

The widely-used compilation of experimental diffusion coefficients by Tyn and Gusek [2] was examined [1, supporting information]. This set — ranging from ribonuclease, 12640 Da, to tobacco mosaic virus, 50 MDa — was plotted as *D* versus log *MW*. The obviously linear species were removed, and values of *D* and *MW* for the outliers were examined. The plot yields a cloud of values of *D* versus log *MW*. In such a plot, rigorously scalable tracers would give a single smooth curve of *D* versus log *MW*. The extent of the cloud represents scatter due to nonscalablity and experimental error. Published values of *D* from hydrodynamic calculations by various laboratories are remarkably consistent with the cloud.

The cloud prediction is certainly good enough for semi-quantitative estimates or for finding the camera frame rate required in single-particle tracking experiments. For globular proteins of known structure, highly accurate values can be obtained from simulations, if required. For a diffusion-controlled reaction in dilute solution, the cloud prediction is close enough that the standard analysis of propagation of errors can be used. But scalable tracers may be useful for diffusion measurements in cytoplasm, in particular to control surface interactions with cytoplasmic components. Geometric scalability would be essential in a measurement of the percolation threshold of cytoplasm.

The incomplete examination of the question here indicates what would be required for a complete examination. (Supported in part by NIH grant GM038133)

References

[1] M .J. Saxton: *Wanted: Scalable Tracers for Diffusion Measurements*. J Phys Chem B **118**, 12805-12817 (2014).

[2] M. T. Tyn, T. W. Gusek: *Prediction of Diffusion Coefficients of Proteins*. Biotech Bioeng **35**, 327–338 (1990).