Living cells have complex and multiscale non-equilibrium environments, with 30 to 40% (by weight) of the cells being composed of macromolecular components: this macromolecular crowding can affect stability, translational motions and chemical kinetics. Theoretical models of macromolecular crowding necessarily introduce simplifications in order to elucidate the most essential features of the environment, the starting point being the role of excluded volume. Experimental model systems are useful because they can play a role that is intermediate to that of both the in-cell environments and the theoretical models.

In our research at Memorial, we begin by examining a simple model system consisting of a probe polymer, polyethylene glycol, and a polysucrose crowder macromolecule (Ficoll-70), using multiple experimental modalities: NMR, rheology and small-angle neutron scattering. We find, above a characteristic concentration, that the polymers exhibit a universal exponential decrease in the translational diffusivity as a function of their concentration [1]. We believe that this universal behaviour could be characteristic of a broad crossover between dilute system behaviour and the scaling behaviour expected in semi-dilute solutions. We then explore the nature of the Ficoll (and other) crowders, and find that the volume they exclude has been hugely underestimated – the Ficolls trap a quantity of bound water that is equal to or larger than their own weight [2]. Finally, we find that, while Ficoll solutions are Newtonian at all relevant concentrations, solutions made from lysed cells are profoundly non-Newtonian, behaving like fluids that require a minimal stress to yield, and whose viscosity decreases with shear rate [3]. Thus, even these simplified experimental model systems raise interesting questions.

**Figure 1:** (a) Diffusivity: Universal linear decrease of In(D) vs concentration c_p in PEG-Ficoll solutions. (b) The effective volume fraction $\phi_{eff}$ (including bound water) is more than twice larger than the specific volume fraction $\phi_s$ occupied by the Ficoll crowder.

**References**

