P.08 Modelling the transport of nanoparticles across the blood-brain barrier

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The blood-brain barrier (BBB) presents a physical barrier to the exchange of almost all molecules between the brain and the blood, restricting nearly all entry to the central nervous system (CNS) to via tightly regulated transport mechanisms. This presents a significant bottleneck in therapeutic intervention for neurological diseases, as >98% of small molecules and ~100% of large molecules are unable to access the brain tissue (Pardridge, 2005). Therefore, a coordinated strategy is required for the encapsulation and specific delivery of therapeutic molecules across the BBB. Recent interest has focused on the use of nanoparticles, functionalised to target natural transport mechanisms across the BBB, for delivery to the CNS. However, enhancing the properties of nanoparticles for optimal uptake requires rigorous testing of their physical and biological interactions. Furthermore, common *in vitro,* transwell models of the BBB, frequently used in the study of trans-BBB delivery, often demonstrate wide discord to *in vivo* models. We have constructed computational models of both *in vitro* transwells and *in vivo* capillaries. These models include considerations for nanoparticle behaviour under blood flow, particle-cell interactions and subsequent transport of particles. This permits the rapid screening of different nanoparticle compositions and moreover, helps explain disparity between *in vitro* and *in vivo* data.

[1] PARDRIDGE, W. M. 2005. The blood-brain barrier: bottleneck in brain drug development. *NeuroRx : the journal of the American Society for Experimental NeuroTherapeutics,* 2, 3-14