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**Theory of margination and cell-free layer thickness in blood flow**

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A mechanistic model is developed to describe segregation in confined multicomponent suspensions such as blood during Couette or plane Poiseuille flow. We focus attention on the case of a binary suspension with a deformable primary component (e.g. red blood cells) that completely dominates the collision dynamics in the system. The model captures the phenomena of depletion layer formation and margination observed in confined multicomponent suspensions of deformable particles. The depletion layer thickness of the primary component is predicted to follow a master curve relating it in a specific way to confinement ratio and volume fraction. Results from experiments and detailed simulations with different parameters (flexibility, viscosity ratio, confinement) collapse onto this curve with only one adjustable parameter. In a binary suspension, several regimes of segregation arise, depending on the value of a "margination parameter" $M$. Most importantly, in both Couette and Poiseuille flows there is a critical value of $M$ below which a sharp "drainage transition" occurs: one component is completely depleted from the bulk flow to the vicinity of the walls. Direct simulations also exhibit this transition as the size or flexibility ratio of the components changes.