A Biomechanics Model of Endocytosis

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Endocytosis is utilized by eukaryotic cells to perform a wide range of functions including the uptake of extracellular nutrients and the regulation of cell-surface receptors, as well as by toxins, viruses, and microorganisms to gain entry into cells. One of the most important endocytic mechanisms is receptor-mediated, whereby the plasma membrane binds specific macromolecules and smaller particles via specialized receptors, invaginates around those particles, and then pinches off to form small vesicles. Receptor-mediated endocytosis had been thought to be assisted by specific proteins, either clathrin or caveolin, polymerizing into a spherical shell around the invagination. Recently however, evidence has arisen for another, clathrin- and caveolin-independent route by which endocytosis may occur. The understanding and quantitative analysis of the mechanics underlying receptor-mediated endocytosis has important implications to not only viral pathogenesis, but also the delivery of macromolecules and nanoparticles for intracellular imaging and targeted therapies.

We have developed an analytic model of endocytosis by considering a particle displaying immobilized ligands gradually attracting and binding receptor proteins on a plasma membrane. The initial binding event nucleates a patch of bound receptors which holds the particle to the membrane. Unbound (free) receptors on the plasma membrane diffuse towards the edge of the patch and bind particle ligands there, bringing more of the membrane into contact with the particle, until the entire particle is engulfed by the plasma membrane. It is assumed that equilibrium is reached between bound and free receptors at the boundary of the contact zone, whenever receptor diffusion is rate-limiting. Using this model, good estimates of minimum radius R_{min} for wrapping and the time t_c required for fully enveloping and ingesting the particle were obtained, and the corresponding scaling laws were given. This simple model is applicable to a wide range of biological problems involving particle internalization, including endocytosis, viral entry and the cellular delivery of nanoparticle probes,