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Stochastic nature of clathrin-coated pit assembly ANAND BANERJEE, ALEXANDER BEREZHKOVSKII, RALPH NOSSAL, National Insitutes of Health — Clathrin-mediated endocytosis is a complex process through which eukaryotic cells internalize various macromolecules (cargo). The process occurs via the formation of invaginations on the cell membrane, called clathrin-coated pits (CCPs). The dynamics of CCP formation shows remarkable variability. After initiation, a fraction of CCPs, called "productive pits", bind to cargo and then grow and mature into clathrin-coated vesicles (CCVs). In contrast, a large fraction of CCPs, called "abortive pits", fail to bind to cargo, grow only up to intermediate sizes and then disassemble. There is notable heterogeneity in the lifetimes of both productive and abortive pits. We propose a stochastic model of CCP dynamics to explain these experimental observations. Our model includes a kinetic scheme for CCP assembly and a related functional form for the dependence of free energy of a CCP on its size. Using this model, we calculate the lifetime distribution of abortive pits (via Monte Carlo simulation) and show that the distribution fits experimental data very well. By fitting the data we determine the free energy of CCP formation and show that CCPs without cargo are energetically unstable. We also suggest a mechanism by which cargo binding stabilizes CCPs and facilitates their growth.

Anand Banerjee
National Insitutes of Health

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