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Modeling Nucleation and Kinetics of Clathrin Assembly by Membrane Localization[1] SIKAO GUO, MARGARET JOHNSON, TC Jenkins Department of Biophysics, Johns Hopkins University — The formation of clathrin lattices on the plasma membrane of cells is a multi-component assembly process which plays an essential role in transport across the membrane. Here we develop a microscopic model that can quantitatively reproduce recent in vitro fluorescence experiments, establishing how cooperativity due to both 2D membrane localization and adaptor protein interactions are necessary to drive the nucleation and growth of clathrin cages. This model is also consistent with the known biochemistry of protein interactions. We simulated this model using the structure-resolved reaction-diffusion simulator NERDSS, collecting minutes-long movies of the clathrin assembly on the membrane. We then show how changing the stickiness of the membrane controls the nucleation of clathrin-coated structures on the surface, with clathrin present now at physiologic concentrations. With this model, we can predict how tuning the stoichiometry of components will impact the nucleation and stability of clathrin cages on membranes, resulting in productive or abortive assembly events. This model and corresponding simulations provide a critical quantitative framework for investigating how the selection of cargo at membranes by associated adaptors controls the speed and success of vesicle formation.

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