

**UNIVERSITY OF SOUTH FLORIDA  
DEPARTMENT OF PHYSICS**

**COLLOQUIUM**

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PHY 130

**A Physical Model of Clathrin Basket Assembly**

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**ABSTRACT**

Clathrin is a major component of the protein coat of plasma-membrane derived vesicles involved in the uptake, into eukaryotic cells, of various substances by a process called "receptor-mediated endocytosis." Among the materials entering by this mechanism are certain critical metabolites, small viruses, and cell-surface receptors targeted for intracellular processing. Clathrin is purified from cell-derived coated vesicles in the form of a heteropolymer (MW ca. 630 KDa) consisting of three clathrin heavy chains joined at a common hub, each heavy chain containing an associated clathrin light chain. These structures, known as "clathrin triskelions," can spontaneously assemble into closed nanoscopic cages (or "baskets"), whose sizes (ca. 100 +/- 20 nm) and extent of polymerization depend on the properties of the solution in which the triskelions are suspended. Basket assembly can be accelerated by the presence of various cell-derived clathrin-associated proteins.

We postulate a simple physical model to explain cage formation. The main premise is that basket assembly is governed by favorable, attractive, inter-leg associations between triskelions, acting in competition with unfavorable triskelion shape distortions and entropic changes that occur when triskelions leave solution to form the baskets. In its simplest form, the model contains three parameters: a rigidity coefficient, a parameter related to the natural curvature (pucker) of an isolated triskelion in solution, and the net energy of enthalpic interactions between the legs. We find that the model provides good fits to data on size distributions of assembled cages, allowing estimates of the magnitudes of these parameters. Analysis of information independently acquired from isolated triskelions by electron microscopy, static and dynamic light scattering, and small angle neutron scattering substantiate the tenets of the model. Application of micellization theory to the model predicts the existence of a critical triskelion concentration that needs to be surpassed before basket assembly can proceed. Parametric analysis, coupled with small angle neutron scattering studies, indicates that inter-leg associations are likely to be the most important factor determining whether triskelions will form stable baskets.