Nonlocal Mechanism of Self-Organization and Centering of Microtubule Asters

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Abstract Fragments of fish melanophore cells can form and center aggregates of pigment granules by dynein-motor-driven transport along a self-organized radial array of microtubules (MTs). We present a quantitative model that describes pigment aggregation and MT-aster self-organization and the subsequent centering of both structures. The model is based on the observations that MTs are immobile and treadmill, while dynein-motor-covered granules have the ability to nucleate MTs. From assumptions based on experimental observations, we derive partial integro-differential equations describing the coupled granule–MT interaction. We use scaling arguments and perturbation theory to study the model in two limiting cases. The model analysis explains the mechanism of aster self-organization as a positive feedback loop between motor aggregation at the MT minus ends and MT nucleation by motors. Furthermore, the centering mechanism is explained by the spontaneous nucleation of MTs throughout the cytosol which acts as a volume sensing tool. Numerical simulations lend additional support to the analysis. The model sheds light on role of polymer dynamics and polymer–motor interactions in cytoskeletal organization.

Keywords Microtubule asters · Molecular motors · Cytoskeleton · Self-organization · Nonlocal mechanism

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1. Introduction

Many fish and amphibia are able to change skin color rapidly for camouflage or to establish dominance. These changes are possible due to the transport of small organelles, referred to here as pigment granules, within specialized cells called melanophores. The change in color of these cells is derived from transport of the granules to and from the cell center (Bray, 2002; Nascimento et al., 2003). When the pigment is dispersed throughout the cytoplasm, it absorbs light, and the cell appears colored. When the granules aggregate at the center, most of the cytoplasm is transparent to light, and the cell appears colorless.

Within each melanophore, thousands of pigment granules are transported during these color changes. This movement relies on the association of the granules with multiple molecular motors that are able to transduce the chemical energy of ATP hydrolysis into mechanical force generation and movement (Bray, 2002). These motors transport the granules along two kinds of linear polymers—actin and microtubules (MTs) that are organized into a cytoskeleton meshwork that determines cell shape and is required for movement (Bray, 2002). Both kinds of polymers are polar, with so-called minus ends and plus ends displaying distinct structure and kinetics. One important type of dynamic behavior, when the rates of polymer subunit assembly onto the plus ends and disassembly from the minus ends are equal, is called treadmilling. A treadmilling polymer translocates in space in the direction of its plus end despite the fact that the subunits embedded in the polymer remain fixed in space. The movement is rather due to the diffusion in the cytoplasm of the subunits disassembling from the minus end and assembling onto the plus end.

While actin polymers are short, disordered and responsible for the dispersion of the granules, MTs are long and ordered into the radial array called a MT aster (Kellogg et al., 1994), in which the minus ends are focussed at the cell center and plus ends extend outward to the cell boundary (Fig. 1). This structure is crucial for pigment aggregation at the cell center, because some of the motor molecules coating the granules are cytoplasmic dynein motors which, when activated, glide toward MT minus ends (Holzbaur and Vallee, 1994).

MT aster formation is normally attributed to the capacity of the specialized organelles—centrosomes—to nucleate and stabilize the MT minus ends (Schiebel, 2000). The central position of the centrosome is actively maintained in living cells, and recent work indicates that an important role in this centering is played by forces generated by molecular motors and MT polymerization (Burakov et al., 2003). However, remarkably, polar MT arrays can self-organize and center in the absence of centrosomes (Verde et al., 1991; Nedelec et al., 1997). The model of aster formation suggested in (Verde et al., 1991) is based on the ability of multivalent minus-end directed motor complexes to associate with two or more MTs simultaneously and to stay attached to a MT upon reaching its minus end. The model asserts that MT minus-end focusing is achieved by the simultaneous motor driven transport of each MT to the minus ends of the other MTs attached to the same motor complex. Centering can be explained by the balance of length-dependent MT buckling forces which is achieved when the focal point of the MT aster is at the center (Nedelec et al., 1997; Tran et al., 2001). These studies