A physical minimalistic model for podosomes

Moshe Naoz[1], Nir Gov[1]

Short Abstract — **Cells produce a variety of protrusions through polymerization of actin filaments near the membrane. Many of these protrusions also contain adhesive proteins that together with the actin filaments organize in a fairly similar way in most adhesive protrusions. I will present a simplified physical model that attempts to explain the structure and behavior of such protrusions (specifically podosomes). In this model, actin activity level depends on membrane curvature as indicated by recent experimental evidence. This dependence can account for some special features observed in these systems.**

***Keywords* — podosomes, actin, adhesion, membrane, curvature.**

PODOSOMES are dynamic actin-rich protrusive adhesion structures formed on the plasma membrane of several cell types. As adhesion structures, podosomes play an important role in cell migration, tissue invasion, extracellular matrix degradation [1]. The podosomes are composed of a rich actin core surrounded by an adhesion ring. In certain cells, at the center of the cylinder there's a tubular invagination of the membrane believed to play a roll in ECM degradation. Podosomes also exhibit higher-order collective structures comprised of many podosomes [2]: a transition from a cluster of uniformly distributed podosomes to an expanding, treadmilling podosome ring structure. The podosome rings eventually coalesce into a stable belt at the cell periphery which is thought to be the precursor of the sealing zone.

The focus of our work is to formulate a theoretical model that describes the formation and dynamics of single podosomes, as well as the large-scale organization of podosomes in clusters and rings. In the model that we propose, we take into account the effects of only a few key podosome components and the forces they exert on the cell membrane. To this end, we greatly simplify the system (which consists of hundreds of protein types and interactions) into three components; each representing a group of proteins contributing to a principal physical function; namely the nucleators of actin filaments (producing protrusive forces), adhesion proteins (that link the membrane to the external substrate) and the cell membrane itself (which induces an elastic restoring force).

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[1]Department of Chemical Physics, Weizmann Institute of science, Rehovot, Israel. E-mail: moshe.naoz@weizmann.ac.il

Recent experiments show a correlation between membrane curvature and actin polymerization [3]. A coupling between actin activity and membrane curvature results in an instability of the membrane-actin system and the initiation of membrane protrusions [4]. In our current model we explore the dynamics of membrane driven by this curvature-actin mechanism, when they are in close proximity to an external substrate which acts as a physical barrier to the membrane's movement.

We first calculate the dynamics of the system without adhesion in order to understand the role of the actin-curvature coupling in the presence of a substrate. This results in two typical behaviors. 1. A single perturbation grows and develops into a cluster of stable protrusions. In the middle of each protrusion we find a local depletion of the actin density, as is observed in the cores of some podosomes. 2. A single perturbation grows but the development of other protrusions is inhibited allowing the main protrusion to transform into an expanding actin ring. The outward expansion of the ring is driven in our model by the same curvature-actin mechanism that acts to initiate the protrusions.

We then add the adhesion component which in addition to linking the membrane to the substrate, also limits the mobility of the actin membrane nucleators. This results in a stable podosome-like structure, containing an actin core with an inwards invagination at the middle, and surrounded by an adhesion ring.

I. Conclusion

The combination of actin-curvature coupling and the proximity to an external barrier (the substrate on which the cell rests) results in rich behavior, namely, expanding rings of actin (in the case of no adhesion), and stable protrusions with an invagination (in the case of adhesion ring). These preliminary results already indicate that the curvature-actin mechanism naturally gives rise to several features of podosomes.

References

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