

MAR17-2016-030167

Abstract for an Invited Paper
for the MAR17 Meeting of
the American Physical Society

Spreading and contraction in phagocytosis: The role of actin organization and curvature¹

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Phagocytosis is the process used by immune cells to engulf and remove foreign objects from the body. The engulfment is realized by the formation of an actin-driven ‘phagocytic cup’ of the cell membrane, which quickly crawls up and then surrounds the object via constriction. In this study, we resolve the paradox of how actin-driven protrusion of the plasma membrane can co-exist with a contractile actin belt proposed to mechanically-drive the closure of the phagocytic cup. To do this we quantitatively assessed macrophage phagocytic behavior in a planar geometry, a process known as frustrated phagocytosis. Our results reveal that phagocytosis occurs in a binary manner, such that once it is initiated, frustrated phagocytosis proceeds at a prescribed rate, resulting in peak contact areas that correspond to a roughly 225% increase in apparent cell surface area. Upon reaching their maximum area, the majority of macrophages enter a period of late-stage contraction. During the contraction phase, cells exert significant stress on the underlying substrate. Contraction also corresponds with dramatic reorganization of the F-actin cytoskeleton, in particular the formation of a bundled contractile belt around the cell perimeter. In contrast to other studies of phagocytosis, our work definitively illustrates that whatever signals trigger late-stage phagocytic contraction must be independent of particle size and curvature. Mounting evidence suggests that membrane tension is involved in late-stage signaling. The idea that tension is linked to late-stage contraction is reinforced by our finding that the peak-contact area roughly corresponds to the area threshold that results in increased cortical tension, as measured by Lam et al., and that reducing tension through hypertonic buffer shock enables the cells to spread further before the onset of contraction.

¹Supported by NSF Grants PHYS-0848797 and SRN-POLS 1205878.