

Alexandra Jilkine, University of Arizona, Tucson, AZ, USA
Andrew R. Houk, University of California San Francisco, San Francisco, CA, USA
Cecile O. Mejean, Yale University, New Haven, CT, USA
Rostislav Boltyanskiy, Yale University, New Haven, CT, USA
Eric R. Dufresne, Yale University, New Haven, CT, USA
Sigurd B. Angenent, University of Wisconsin, Madison, WI, USA
Steven J. Altschuler, Southwestern Medical School, Dallas, TX
Lani F. Wu, Southwestern Medical School, Dallas, TX, USA
Orion D. Weiner, University of California San Francisco, San Francisco, CA, USA

Discriminating between models of neutrophil polarity through cell severing and perturbations of cell geometry

Many eukaryotic cells polarize and migrate, either spontaneously, or in response to external chemoattractant. Polarity is characterized by a rapid conversion from a round to an elongated morphology, with a leading lamellipod at the front. A widespread assumption is that the leading edge prevents formation of multiple fronts by generating long-range diffusible inhibitors or by sequestering essential polarity components. Experiments with tethered neutrophil-like cell line show that even cells with drastically altered “dumbbell” geometries still establish a unique front. Severing experiments, where a cell fragment is able to form a new axis of polarity, indicate that there is long range communication between the front and back of the cell that prevents the formation of multiple fronts.

However, we show that when cell geometry is altered, several proposed classes of reaction-diffusion (RD) models for polarity establishment either give rise to multiple fronts or are not able to re-animate upon severing. This allows us to show that proposed diffusion-based mechanisms are not sufficient for long-range inhibition by the pseudopod. We find that membrane tension doubles during leading-edge protrusion, and increasing tension is sufficient for long-range inhibition of multiple fronts. Furthermore, reducing membrane tension causes multiple pseudopods. We suggest that tension, rather than diffusible molecules generated or sequestered at the leading edge, is the dominant source of long-range inhibition that constrains the spread of the existing front and prevents the formation of secondary fronts.