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Antibody-mediated immobilization of virions in mucus. (English) Zbl 1427.92035

Bull. Math. Biol. 81, No. 10, 4069-4099 (2019).

Summary: Antibodies have been shown to hinder the movement of herpes simplex virus virions in cervicovaginal mucus, as well as other viruses in other mucus secretions. However, it has not been possible to directly observe the mechanisms underlying this phenomenon, so the nature of virion-antibody-mucin interactions remain poorly understood. In this work, we analyzed thousands of virion traces from single particle tracking experiments to explicate how antibodies must cooperate to immobilize virions for relatively long time periods. First, using a clustering analysis, we observed a clear separation between two classes of virion behavior: freely diffusing and immobilized. While the proportion of freely diffusing virions decreased with antibody concentration, the magnitude of their diffusivity did not, implying an all-or-nothing dichotomy in the pathwise effect of the antibodies. Proceeding under the assumption that all binding events are reversible, we used a novel switch-point detection method to conclude that there are very few, if any, state switches on the experimental timescale of 20 s. To understand this slow state switching, we analyzed a recently proposed continuous-time Markov chain model for binding kinetics and virion movement. Model analysis implied that virion immobilization requires cooperation by multiple antibodies that are simultaneously bound to the virion and mucin matrix and that there is an entanglement phenomenon that accelerates antibody-mucin binding when a virion is immobilized. In addition to developing a widely applicable framework for analyzing multistate particle behavior, this work substantially enhances our mechanistic understanding of how antibodies can reinforce a mucus barrier against passive invasive species.

MSC:

92C30 Physiology (general)
62P10 Applications of statistics to biology and medical sciences; meta analysis

Keywords:

mucosal immunology; particle tracking; switching diffusion; uncertainty quantification

Software:

clusfind; R; S-PLUS

Full Text: DOI

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