Fusion and fission events regulate endosome maturation and viral escape

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Abstract-

Endosomes are intracellular vesicles that mediate the communication of the cell with its extracellular environment. They are an essential part of the cell’s machinery regulating intracellular trafficking via the endocytic pathway. Many viruses, which in order to replicate require a host cell, attach themselves to the cellular membrane; an event which usually initiates uptake of a viral particle through the endocytic pathway. In this way viruses hijack endosomes for their journey towards intracellular sites of replication and avoid degradation without host detection by escaping the endosomal compartment. Recent experimental techniques have defined the role of endosomal maturation in the ability of enveloped viruses to release their genetic material into the cytoplasm. Endosome maturation depends on a family of small hydrolase enzymes (or GTPases) called Rab proteins, arranged on the cytoplasmic surface of its membrane. Here, we model endosomes as intracellular compartments described by two variables (its levels of active Rab5 and Rab7 proteins) and which can undergo coagulation (or fusion) and fragmentation (or fission). The key element in our approach is the “per-cell endosomal distribution” and its dynamical (Boltzmann) equation. The Boltzmann equation allows us to derive the dynamics of the total number of endosomes in a cell, as well as the mean and the standard deviation of its active Rab5 and Rab7 levels. We compare our mathematical results with experiments of Dengue viral escape from endosomes. The relationship between endosomal active Rab levels and pH suggests a mechanism that can account for the observed variability in viral escape times, which in turn regulate the viability of a viral intracellular infection.

Index Terms-

Citation:

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