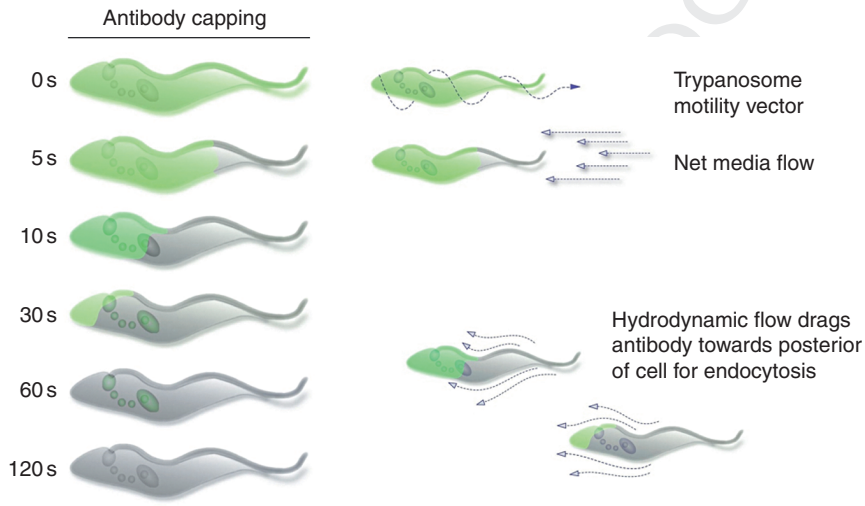
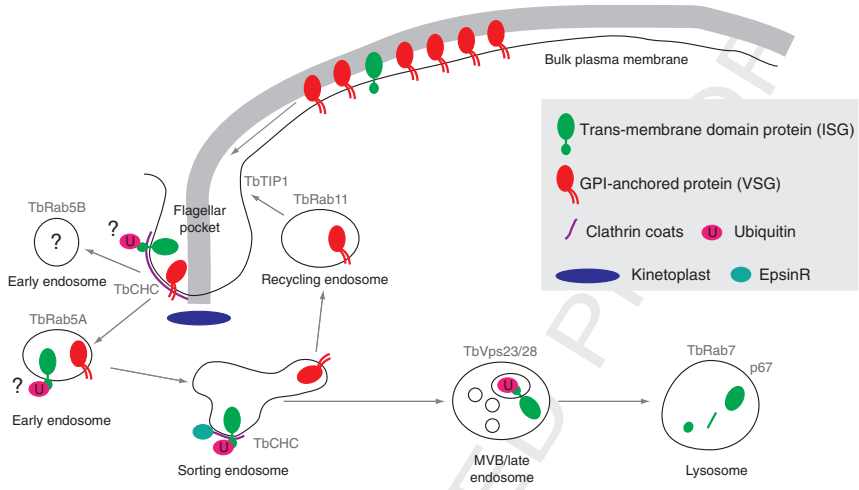


Mark C. Field et al., Figure 1.2 Immune evasion by antibody capping; a role for hydrodynamic flow. Left column: Antibody recognizing the surface variant surface glycoprotein (VSG) is rapidly capped toward the posterior of the cell. The high rate of endocytosis facilitates efficient uptake of the antibody, which is ultimately degraded; the uptake process, even in the presence of high antibody titers, can be completed within 2 min. Right column: Trypanosomes continuously swim, and thereby generate directional flow fields on their cell surface. These flow forces become more significant when the surface VSG is recognized by immunoglobulins. Antibody–VSG complexes are pulled by hydrodynamic forces toward the rear of the cell, where they are endocytosed. This implies that purely physical forces can sort proteins in the plane of the plasma membrane. The schematic shows antibody in green coating VSG in gray.



Mark C. Field et al., Figure 1.3 A model of sorting of GPI-anchored and trans-membrane domain proteins in trypanosomes. Trans-membrane domain proteins such as ISGs (green) are present at low density at the cell surface in comparison to the dominant GPI-anchored VSG (red). There is presently no evidence that there is selective partitioning of GPI versus trans-membrane anchored proteins at the cell surface. Endocytosis requires the function of clathrin (purple) at the flagellar pocket, and for ISG65 and VSG, this serves to target the molecules to the Rab5A-positive early endosome. VSG is segregated at the sorting endosome, and is excluded from a clathrin-tagged membrane microdomains; it is hypothesized that clathrin may actively sort trans-membrane domain proteins at this location, via recognition of ubiquitylated cargo (pink lozenge); this may involve the trypanosome epsin-related protein, which interacts with clathrin (cyan lozenge). Recycled molecules are returned to the cell surface via a Rab11-dependent pathway that also involves a coiled-coil Rab11-interacting protein that likely serves as a docking site at the flagellar pocket. Trans-membrane domain cargo is delivered to the lysosome via the multivesicular body, and degraded. This latter pathway depends on functioning of the ESCRT complex, including TbVps23. The site(s) where ubiquitin is added are unknown. Also the model assumes that all GPI-anchored proteins are recycled and all trans-membrane domain proteins are directed to the lysosome—this is unlikely to be the case, but data concerning trafficking of additional factors are not available at this time. Finally, the function of the Rab5B endosome remains mysterious as besides the presence of lactosamine-repeat determinants, the identity of the molecules transported via this route are unidentified.