Ever since electron microscopy became an important tool in the scientific research, the focus had been mainly on ultrastructural analysis with little success in the development and application of suitable techniques for the localization of macromolecules in cells. The emergence of immunogold techniques in the 1960s managed to fill this gap in serving this function. The aim of this chapter is to equip researchers, postgraduate students, and technicians with essential knowledge to utilize immunogold techniques for ultrastructural investigations in the life sciences. The principles and factors in SUMMARY Electron microscopy, considered by some to be an old technique, is still on the forefront of both clinical viral diagnoses and viral ultrastructure and pathogenesis studies. In the diagnostic setting, it is particularly valuable in the surveillance of emerging diseases and potential bioterrorism viruses. In the research arena, modalities such as immunoelectron microscopy, cryo-electron microscopy, and electron tomography have demonstrated how viral structural components fit together, attach to cells, assimilate during replication, and associate with the cellular machinery during replication. 