A critical step in the biosynthesis of many proteins involves either translocation across a cellular membrane or integration into a cellular membrane. Both processes proceed via the Sec translocon - a ubiquitous and highly conserved transmembrane channel. Recent structural studies offer high-resolution snapshots of the translocon, and a wealth of biochemical and genetic data indicate important residues within the translocon; but many fundamental aspects of its mechanism and regulation remain unclear. Using both atomistic simulations and coarse-grained modeling, we investigate the conformational landscape and long-timescale dynamics of the translocon, and we explore the role of peptide substrates in the regulation of the translocation and integration pathways. Implications of these results for the regulation of Sec-mediated pathways for protein translocation, membrane integration, and integral membrane protein expression are discussed.