Macromolecule drugs such as insulin have transformed our capacity to effectively treat diseases; however, their rapid degradation and poor absorption in the gastrointestinal (GI) tract generally limits their administration to parenteral routes. An oral biologic delivery system must aid in both localization and permeation to achieve systemic drug uptake. In this thesis I will describe two oral capsules designed to systemically deliver macromolecules by inserting the drugs directly into the walls of the gastrointestinal tract. One device is designed to deliver to the stomach wall, while the other device is designed to deliver to the wall of the small intestine. Ex vivo studies on human GI tissue and in vivo studies in rats and swine support the devices’ safety and high delivery efficiency. I perform a cost effectiveness analysis using a first and second order Monte Carlo simulation to show that these new methods of oral macromolecule delivery should increase the quality-adjusted life expectancies of patients suffering from diabetes. Moreover, I demonstrate that electronic systems can be incorporated into these devices for communication and additional therapeutic applications. With the ability to load a multitude of drug formulations, the devices can serve as platform technologies to orally deliver therapeutic doses of macromolecule drugs.