This thesis aims to develop comprehensive sustainability assessment frameworks to analyze sustainability impacts of alternative vehicle technologies in the U.S. To realize this goal, a series of knowledge gaps are identified and problem-driven methodologies are proposed to fill these research gaps. This dissertation is composed of four main sections, each proposing a system-specific decision-making framework and answering crucial research questions for the U.S. transportation sustainability. First section analyzes the state-specific carbon and energy footprint of the alternative vehicle technologies considering spatial and temporal variations in electric power generation and driving patterns. In the second section, the same methodology is applied to reveal state-specific water consumption and withdrawal of alternative vehicle technologies. In the third section, system dynamics modeling approach is utilized to model the U.S. transportation sector and its dynamic interactions with economy, the environment, and society, which capture feedback mechanism, complexity, and temporal dimensions. In the fourth section, the proposed system dynamics model is improved by the consideration of inherent uncertainties associated with the U.S. transportation. The outcomes of this research will advance the state-of-the-art and state-of-the-practice in sustainability research by presenting novel approaches to deal with the problems associated with the U.S. transportation sustainability. This thesis can advance scientific understanding of the triple bottom line (Environment, Society, and Economy) interactions with the U.S. transportation by developing integrated system-based sustainability assessment frameworks for the use of policy makers, industry stakeholders, and researchers worldwide to disseminate the sustainability knowledge and contribute to the further multidisciplinary sustainability researches.