This thesis focuses on the development of a flexible, physics-based life prediction approach for steels under complex conditions. Low alloy steels continue to be the materials of choice for large turbomachinery structures experiencing high temperatures for long durations. There has been significant advancement in the research of modern alloys; however, these materials are still utilized in boilers, heat exchanger tubes, and throttle valve bodies in both turbomachinery and pressure-vessel/piping applications. The material 2.25Cr-1Mo is studied in the present work. The resistance of this alloy to deformation and damage under creep and/or fatigue at elevated temperatures make it appropriate for structures required to endure decades of service. Also, this material displays excellent balance of ductility, corrosion resistance, and creep strength under aggressive operating conditions. Both creep and thermomechanical fatigue conditions have been the limiting factor for most turbine components fabricated from various alloys; therefore, a life prediction approach is constructed for simulating fatigue life for cases where the material is experiencing mechanical loading with thermal cycling. Flexibility is imported to the model through its ability emphasize the dominant damage mechanism which may vary among alloys. A material database is developed to improve and compare the model with experimental data. This database contains low cycle fatigue (LCF), creep fatigue (CF), and thermomechanical fatigue (TMF) experiments. Parameters for the model are obtained with regression fits in comparison with the broad experimental database. Additionally, the cumulative damage approach, better known as Miner’s rule, is used in this study as the fundamental method to combine damage mechanisms. Life predictions are obtained by the usage of a non-interacting creep-plasticity constitutive model capable of simulating not only the temperature and rate dependence.