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A fundamental understanding of how oxide materials respond when exposed to the extreme conditions characteristic of advanced nuclear energy systems is essential to the development of nuclear fuels, structural materials, and waste forms. Material challenges include radiation damage, high-temperature fields, complex mechanical stresses, severe chemical environments, and ageing. Indeed, a more complete and mechanistically based understanding of microstructural and microchemical evolution in fuels and structural materials under irradiation can provide a fundamental basis for developing and predicting the behaviour of advanced fuels with the potential for outstanding fuel performance capable of performing to high radiation doses at high temperatures. This would enable the design of advanced nuclear energy systems that can operate with increased reliability and safety, and with improved economics. To successfully meet these challenges, development of new experiments describing the atomic and mesoscopic organisation, improvement of the modelling of electronic structures, and establishing a theoretical frame to link them are all required. Materials of interest to advanced nuclear energy systems include the fuel itself, but also materials used to clad the fuel, to fabricate other structural components of the reactor, and to engineer stable waste forms. The common thread among these many materials and applications is the relationship between materials microstructure and the physical and mechanical properties of the material. Despite the vast differences in properties and functionality of these disparate materials systems, they share a common link of microstructural evolution in response to atom displacements and radiation damage. For oxide systems, the initial, nearly homogeneous composition often evolves into a multiphase, multicomponent material as new chemical species are produced by fission or chemical segregation in an environment of high radiation flux and high-temperature gradients. In this presentation we would like to review a few model systems (uranium oxides, transition metal oxides, …) where microstructural and chemical changes lead to substantial changes in physical properties, mechanical instabilities, and formation of non-equilibrium phases.