Diagnosis and, when possible, prognosis of faults are essential for safe and reliable operation. The area of fault diagnosis has emerged over three decades. The majority of studies related to linear systems but real-life systems are complex and nonlinear. The development of methodologies coping with complex and nonlinear systems have matured and even though there are many un-solved problems, methodology and associated tools have become available in the form of theory and software for design. Genuine industrial cases have also become available. Analysis of system topology, referred to as structural analysis, has proven to be unique and simple in use and a recent extension to active structural techniques have made fault isolation possible in a wide range of systems. Following residual generation using these topology-based methods, deterministic and statistical change detection has proven very useful for on-line prognosis and diagnosis. For complex systems, results from non-Gaussian detection theory have been employed with convincing results. The paper presents the theoretical foundation for design methodologies that now appear as enabling technology for a new area of design of systems that are reliable in practise. Yet they are also affordable due to the use of fault-tolerant philosophies and tools that make engineering efforts minimal for their implementation. The paper includes examples for an autonomous aircraft and a baling system for agriculture.