Improvements in semiconductor process technology have allowed chip designers to deliver ever more powerful systems while simultaneously lowering system costs. However, recent trends in power dissipation, reliability, thermal constraints, and device variability threaten to limit the performance growth and increase system costs in future microprocessors. Due to the temporal and spatial nature of many of these technology-related problems, designers can achieve the largest impact by addressing these issues at all levels of the hierarchy. In this talk, I will outline several projects in my research group that seek to address these issues for embedded and high-performance systems. These projects include efforts in the areas of a) power and performance modeling and design for future chip-multiprocessor systems, b) joint hardware and software approaches to address delta-V induced soft errors, and c) micro architectures that are designed to cope with device variability. I will focus on recent work that seeks to utilize statistical inference models to rapidly estimate the power and performance of large microprocessor design space.