I will present work that links mechanistic, mathematical models with big-data approaches to address fundamental questions about vascular structure, blood flow, and how vital rates like metabolic rate and growth rate scale across species. Recent progress on these questions has been enabled by new software developed in my group for automatically measuring the dimensions, geometry, and topology of blood vessels from three-dimensional images (e.g., CT and MRI). This software (angicart) leads to much faster collection of larger amounts of data than was previously possible. Based on data obtained from the application of this software, I describe the identification of new patterns for the asymmetry and self similarity of vascular branching. I also explain attempts to develop new models for the structure and dynamics of vascular networks, and intriguingly I show results from analyses that explore whether biological and physical constraints in real organisms exist at the level of the whole network or of individual branching nodes.