

Jessica Leete

Computational Biology and Bioinformatics

PhD Thesis

Heart disease is the leading cause of death in adult Americans today. Hypertension is a major risk factor for heart disease; however, rates of hypertension and how well prescribed drug treatments control hypertension varies by sex. Using published data on known physiological sex differences in the renin-angiotensin system and kidney function. I created sex specific computational models of blood pressure regulation. systems of ordinary differential equations These described cardiovascular function, renal hemodynamics, renal tubular transport, and the renin-angiotensin system. Using these models, I investigated how known physiological sex differences translate into differences in drug treatment efficacy for common antihypertensive Furthermore, I applied these models to drugs. investigate how potential risk factors can increase the risk of acute kidney injury in patients undergoing antihypertensive treatment.

Sex-specific Computational Models of Blood Pressure Regulation

Building these models required parameter fitting from published experimental data, parameter sensitivity analysis, and validation with drug treatment data before exploring new hypotheses. The renin-angiotensin system submodel is a set of differential equations based on first order reaction rate kinetics, where reaction rate constants were solved for using steady state assumptions and published peptide levels. Both the steady state solution and time dependent simulations were numerically computed and analyzed to understand the effects of angiotensin converting enzyme inhibitors, renin angiotensin receptor blockers, loop diuretics, and nonsteroidal antiinflammatory drugs.

