Healthy kidneys filter wastes from blood and keep body chemicals in balance. When the kidneys fail to perform their functions to full capacity, one cannot live long without some form of renal replacement therapy. One available treatment is hemodialysis, in which the patients' blood is pumped into an artificial kidney where metabolic waste products diffuse out of the blood, and the cleansed blood is then returned back to the body. Most people have 3 dialysis sessions every week, each session for about 3 to 4 hours.

In order to perform hemodialysis, the patient must have suitable vascular access to allow adequate flow of blood to the hemodialysis circuit. The most common types of vascular access used for hemodialysis are the arteriovenous (AV) fistula and the expanded polytetrafluoroethylene (ePTFE) graft. A surgeon creates an AV fistula by directly connecting an artery to a vein, usually in the forearm. The increased blood flow causes the vein to hypertrophy so that it can be used for repeated needle insertions. A graft connects an artery to a vein by using a synthetic tube of ePTFE, usually in the shape of a loop. It does not require as much time to mature as a fistula, so it can be used soon after placement.

Both types of vascular access can have complications that require further treatment or surgery. As a well-functioning vascular access is essential for hemodialysis, extensive morbidity exists among end-stage renal disease (ESRD) patients. How long can someone live on dialysis and how well can someone do, depend heavily on the quality of the medical care. The expense of creating and maintaining vascular access for patients on dialysis accounts for a significant portion of any healthcare system. In the US alone, more than 20% of patients with ESRD are hospitalized for vascular access procedures, at an annual cost of 1 billion dollars.

The leading cause of access failure is from loss of patency due to venous stenosis (50% narrowing of the blood vessel), as the result of neointimal hyperplasia formation either at the site of venous anastomosis or in the downstream vein. It is then of critical importance to detect access stenosis in a timely manner so that appropriate corrective steps can be undertaken prior to thrombosis (total occlusion of the blood vessel). However, while the occurrence of stenosis is well recognized, the pathogenesis of it is complex and still not well understood. The process involves a number of growth factors, migration and proliferation of different types of cells, and excessive production of extracellular matrix. The release of growth factors due to oxidative stress and turbulent flow has been suggested as a possible mechanism for neointimal hyperplasia formation.

At the Mathematical Biosciences Institute, postdoctoral researchers Paula Budu-Grajdeanu and Richard Schugart, together with mathematician Avner Friedman, work closely with the Interventional Nephrology Team of The Ohio State University Medical Center, Anil Agarwal, Chris Valentine and Brad Rovin, to analyze the biological mechanisms that lead to vascular access stenosis and direct attention to potential therapies to prevent and treat stenosis. Using partial differential equations to describe the complex pathogenic network relevant to neointimal hyperplasia formation, they have developed a mathematical model, in which all growth factors (TGF-β, PDGF, ET-1) are lumped together into one generic chemical species and all cellular species (smooth muscle cells, fibroblasts) are lumped together into one generic cell type. The model accounts for oxidative stress by having the growth factors increase as the luminal radius decreases.
This relatively simple model captures some of the main features of intimal hyperplasia formation and it realistically predicts the stenotic event (red line) as a function of the initial concentration of the growth factors inside the intimal-luminal space (black curve). It also shows that a drop in the initial concentration of growth factors delays the access stenosis, prolonging the lifespan of the vascular access (blue curve).

The results imply that one mechanism by which the functional state of the hemodialysis vascular accesses can be extended is to control the concentration of the growth factors in the proximal vein. In particular, interventions aimed at specific chemical mediators involved in VNH formation may be successful in reducing the human and economic costs of vascular access dysfunction. With cooperative efforts, i.e., interplay between computational experiments and data, the mathematical model can be expanded and used by clinical researchers as a testbed for exploring and evaluating various therapies that can target both the traditional and the alternative pathways that are involved in the pathogenesis of vascular stenosis. As only limited empirical data for various parameters is available at present, clinical studies need to be conducted in parallel with the development of the model to improve its reliability.