Convection enhanced delivery is an attractive option for the treatment of several neurodegenerative diseases such as Parkinson, Alzheimer, and brain tumors. However, the occurrence of a backflow is a major problem impeding the widespread use of this technique. In this paper, we analyze experimentally the force impact of high flow microinfusion on the deformable gel matrix. To investigate these fluid structure interactions, two optical methods are reported. First, gel stresses during microinfusion were visualized through a linear polariscope. Second, the displacement field was tracked using 400 nm nanobeads as space markers. The corresponding strain and porosity fields were calculated from the experimental observations. Finally, experimental data were used to validate a computational model for fluid flow and deformation in soft porous media. Our studies demonstrate experimentally, the distribution and magnitude of stress and displacement fields near the catheter tip. The effect of fluid traction on porosity and hydraulic conductivity is analyzed. The increase in fluid content in the catheter vicinity enhances the gel hydraulic conductivity. Our computational model takes into account the changes in porosity and hydraulic conductivity. The simulations agree with experimental findings. The experiments quantified solid matrix deformation, due to fluid infusion. Maximum deformations occur in areas of relatively large fluid velocities leading to volumetric strain of the matrix, causing changes in hydraulic conductivity and porosity close to the catheter tip. The gradual expansion of this region with increased porosity leads to decreased hydraulic resistance that may also create an alternative pathway for fluid flow. [DOI: 10.1115/1.4001164]

Keywords: fluid structure interaction, invasive drug delivery, porous tissue deformation, porosity change, microinfusion
2 Experimental Techniques

2.1 Technique A: Stress Field Visualization Using Photoelasticity. Agarose gel is a transparent porous material, which can be perfused with fluids. Its mechanical properties and hydraulic conductivity are similar to that of the soft brain tissue. Therefore, it has often been used as a brain surrogate [10,11]. The gel solution is prepared by adding 0.6 wt % agarose (Sigma Aldrich A6013) and 0.9 wt % NaCl (Sigma Aldrich S7653) to boiling deionized water. The solution is constantly agitated on a magnetic stirrer until the solution becomes clear [11]. The gel solution is cooled to 50°C, poured into glass chambers with an infusion catheter already in place. The gel cast is allowed to set for about 1 h at room temperature.

The solidified gel possesses the property of photoelasticity or optical anisotropy in stressed state [12]. Thus, the tensor of refractive indices at a stressed material point in stressed state is different from that in an unstressed state. Thus, the refractive index tensor correlates with the stress tensor at each point. When a ray of plane polarized light passes through the photoelastic material, it decomposes into two component waves along the fast and slow axes, which are collinear with the principal stress axes. Each of these two components experiences a different refractive index, which are collinear with the principal stress axes. Each of these components experiences a different refractive index, which are collinear with the principal stress axes. Thus, when viewed through a linear polariscope, the relative retardation is visible as intensity change in the image forming a fringe pattern called isoclinics [13]. The isoclinic pattern shows the locus of all points in the specimen along which the principal stresses are in the same direction. A schematic for the linear polariscope, custom-built to visualize gel stress during microinfusion, is shown in Fig. 2.

\[ \Psi = C \cdot h \cdot (\sigma_{11} - \sigma_{22}) \]

where \( \Psi \) is the induced retardation, \( C \) is the material’s stress optic coefficient, \( h \) is the specimen thickness, and \( \sigma_{11} \) and \( \sigma_{22} \) are the first and the second principal stresses, respectively. When viewed under a linear polariscope, the relative retardation is visible as intensity change in the image forming a fringe pattern called isoclinics [13]. The isoclinic pattern shows the locus of all points in the specimen along which the principal stresses are in the same direction. A schematic for the linear polariscope, custom-built to visualize gel stress during microinfusion, is shown in Fig. 2.

2.1.1 Construction of Linear Polariscope. The polariscope was constructed using two polarizers (NT53–351, Edmund optics), the test chamber (agarose gel), and a digital camera (Canon Digital Rebel XTi EOS 400D, 10 MP), as shown in Fig. 2. Collimated light was obtained by placing a 5 W light emitting diode with a small aperture at the focal distance of an achromatic lens (50 mm focal length, NT27–271, Edmund optics).

2.2 Technique B: Displacement Measurement With Nanobead Space Markers. The second technique quantifies the gel matrix displacement caused by fluid infusion. A schematic for the experiment is shown in Fig. 3. Nanobeads (400 nm diameter, Visiblex from Phosphorex Inc.) were dispersed in a hot gel solution while heating and constantly stirring the mixture at 100 rpm to obtain a homogenous particle distribution. The nanobeads are bigger than the average gel pore diameter of \( d = 100 \) nm [14]. Thus, the nanobeads are robustly embedded into the gel matrix after solidification. Accordingly, any nanobead dislocation corresponds to gel matrix displacement. While infusing water into the gel seeded with nanobeads, consecutive images were taken at different instants of time with the camera (Canon Digital Rebel XTi EOS 400D camera 10 MP) through a microscope (Nikon Eclipse ME600) at 100X magnification.

The displacement field was calculated using a space correlation between two consecutive images [15]. The aim of the correlation is to find the displacement vector field of the nanobead pattern that has moved during the time interval. The motion of the two particle patterns in the two consecutive images gives the desired displacement of the gel matrix. The displacement inside an interrogation window of fixed size, belonging to two consecutive images, can be computed by solving for the vector \( s \), which maximizes the correlation function \( R(s) \). The correlation function \( R(s) \) computes the two-dimensional area integral over the fixed inter-
rogation window, 64 × 64 pixels in size, as shown in Eq. (2). The value of the integral depends on the two components of the vector s, and the convolution of the corresponding intensities distributions, \( I_1(x) \) and \( I_2(x+s) \). The two intensities are taken, evaluated at a specific spatial position: \( x \) for the first image, and the point \( x+s \) in the second image. The two specific components of the vector \( s \) leading to the maximum value of the correlation function give the desired displacement vector for the current interrogation window. A maximum of the correlation function identifies the specific \( s \), as shown in Fig. 4

\[
R(s) = \int_{IW} I_1(x) \cdot I_2(x+s) \, dx
\]  

(2)

The process is repeated for each interrogation window in the domain until the entire displacement field is completely determined. These crude results are further filtered by rejecting values below an appropriate correlation threshold. The final displacement field is computed by scaling with a calibration coefficient to convert pixel dimensions into real spatial dimensions. This correlation procedure can be performed in MATLAB or a commercial software like ISSN DPIV [16,17].

Fig. 3 Schematic and experimental setup for tracking nanobeads seeded in agarose gels during infusion.  

Fig. 4 The space correlation between two interrogation windows (left) yields the displacement vector. Individual nanobeads are represented as circles. To obtain the displacement vector, cross-correlation procedure is executed by maximizing a correlation function (right). Here, coordinates \( s_x \) and \( s_y \) correspond to the displacement vector components along the \( x \) and \( y \) axis.

Fig. 5 The polariscope is held in the dark field mode. The gray box shows the outline of the catheter through which fluid was infused from right to left, as indicated by the arrow: frame (a) before infusion, no isoclinic pattern; (b) infusion begins at high flow rate 5 \( \mu \)l/min, isoclinic fringes start to develop and is seen as a white field; (c) infusion continues and isoclinic fringe pattern can be observed more clearly.