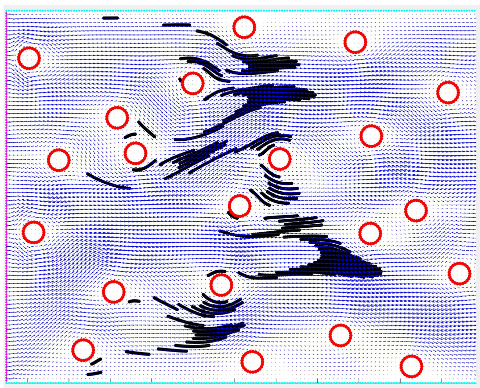
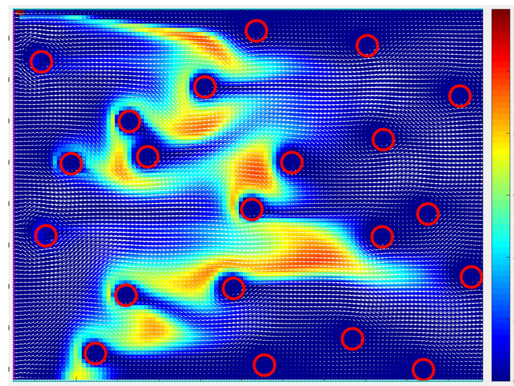
Matlab routines *interstitial_flow_discrete* and *interstitial_flow_continuous* show how drugs (modeled either as discrete molecules or as continuous concentrations) extravasate from the vasculature into the tumor interstitium and are distributed within the tissue due to the advective flow of the interstitial fluid. The final drug distribution after its bolus injection in both cases is shown below:



Distribution of individual drug molecules under the advective transport with the interstitial fluid.



Distribution of a concentration of drug molecules under the advective transport with the interstitial fluid.

The advective transport is determined using the method of regularized Stokeslets [1] with the specific blob function: $\phi_\delta(\mathbf{x})=2\delta^4/(\pi(\|\mathbf{x}\|^2+\delta^2))$. The following algorithm is applied:

1) Define tissue architecture: cell positions and domain size
2) Determine velocities on cell boundaries (immobile, zero), on domain boundaries (zero) and along the vessel (interstitial fluid influx)
3) Compute forces f_{cell} at the cell boundaries and f_{bdn} on the domain boundaries, and f_{in} along the capillary, so that $u_{cell}=0$, $u_{bnd}=0$ and $u_{in}=1$ μm/sec (the computed forces are shown during the run of the routine *interstitial_flow_discrete*)
4) Use forces f_{cell}, f_{bnd} and f_{in} to compute fluid flow in any point in the domain (the cimputed fluid flow on the regular grid is shown by both routines, and is also shown above)
5) This determines the advective transport:
   a) for the individual molecules x_d^n the velocity is $u(x_d^n)$, and molecular movement is described by the Euler method (shown above): $x_d^{n+1}=x_d^n+\Delta t * u(x_d^n)$
   b) for the continuous description $c_{i,j}^n$ the velocity is $(u_{i,j}^n, v_{i,j}^n)$ and the drug transports is described using the upwind method (shown above):

$$c_{i,j}^{n+1} = c_{i,j}^n + (\Delta t/h)\ \{ u_{i,j}^n (c_{i,j}^n - c_{i-1,j}^n) \text{ if } u_{i,j}^n > 0 \text{ or } u_{i,j}^n (c_{i+1,j}^n - c_{i,j}^n) \text{ if } u_{i,j}^n < 0\} +$$
$$\{ v_{i,j}^n (c_{i,j}^n - c_{i-1,j}^n) \text{ if } v_{i,j}^n > 0 \text{ or } v_{i,j}^n (c_{i+1,j}^n - c_{i,j}^n) \text{ if } v_{i,j}^n < 0$$