Resistive-pulse sensing at the micro- and nanoscale

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Outline

- Resistive pulse sensing background
- Mesoscale resistive pulse sensing
    - Resistive pulse sensing of rods
- Microscale resistive pulse sensing
    - Simultaneous imaging and resistive pulse studies
    - Cancer cell deformability cytometry

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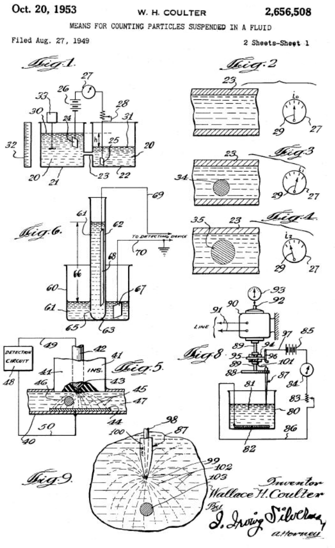
Resistive pulse sensing background

Resistive pulse sensing—description

- Resistive pulse sensing (RP) is a method for single particle detection and characterization
- Works at any scale (nano, micro, milli, etc.)
- A diverse range of applications: red blood cell counting, virus detection, protein conformational change detection, and DNA sequencing



Resistive pulse sensing—how does it work?

- Particles are suspended in a conductive solution, which is injected into a pore/channel system
- An external voltage is applied across the channel, which induces an ionic current—the channel acts as an Ohmic resistor with governing equation $V = IR$, where V is the applied voltage, I the measured current, and R the electrical resistance of the channel
- When a particle enters the channel its resistance changes, yielding a transient change in the measured ionic current
- By studying the properties of the current pulse, particle properties such as size, concentration, charge, and shape may be elucidated

Resistive pulse sensing—the actors at play

1. Particles of interest (**transport mechanisms**, **electrostatic boundary conditions**)
2. The channel itself (surface chemistry and **electrostatic boundary conditions**)
3. Electrolyte solution (**solvent, ion transport**)
4. Electrodes (electrochemical ion-electron current transduction, **voltage source**)

Resistive pulse sensing—the actors at play

- Consider an ionic conducting system consisting of two electrodes placed across a small channel, and immersed in an electrolyte solution with two symmetric ion species of bulk number density n_+ and n_- and valency z (charge $\pm e$ in solution)
- The following equations yield the measured current in the system:

$$I = \oint_{\mathrm{A}} ze\left(n_+\vec{v}_+ - n_-\vec{v}_-\right)\cdot\hat{n}dA$$

- Ion velocity is a combination of *passive* and *active* transport
- Passive transport: Thermal energy and convection (motion coupled to fluid flow
- Active: Electric migration (electric forces)

$$\vec{v}_\pm =$$

Resistive pulse sensing—how does it work?

Diffusion: At finite temperature $T > 0$ ions have thermal energy; if there is a concentration gradient $\nabla n_{\pm}$ in the fluid, a net spontaneous transport of ions from high concentration to low concentration regions will occur with magnitude proportional to the concentration gradient; we can consider the *net* velocity of a single ion to be the mean of the ensemble velocity:

$$\vec{v}_{\pm}^{\text{diffusion}} = \frac{D_{\pm} \nabla n_{\pm}}{n_{\pm}}$$

Migration: Ions in an electric field experience an electric force, which accelerates them until they acquire a final drift velocity given by:

$$\vec{v}_{\pm}^{\text{migration}} = \mu_{\pm} \vec{E}$$

The mobility D_{μ} is related to the diffusion coefficient $D_{\pm}$

Resistive pulse sensing—how does it work?

Convection: If the solvent itself is moving—not just the ions—the fluid velocity will be added to the ion velocity

$$\vec{v}_{\pm}^{\text{convection}} = \vec{u}$$