Differentiating between single particle transport types

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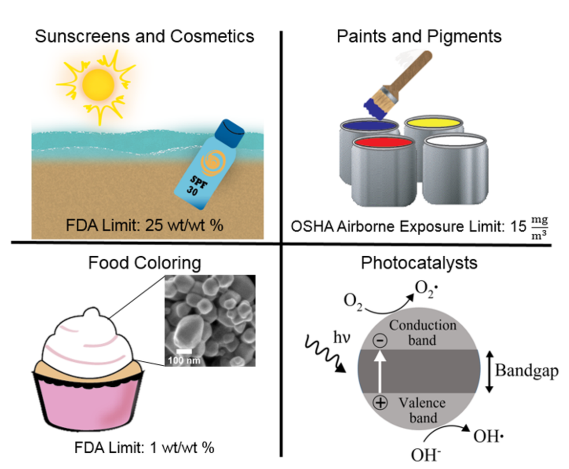
Objectives

- Characterize the types of behaviors that exist for lysosome populations containing and not containing titanium dioxide (TiO_2) nanoparticles.
- Model selection analysis using Bayesian statistics that reports the probability that a path is active, immobile, or free.

Titanium dioxide (TiO_2) nanoparticles

TiO_2 NPs are used as pigments and photocatalysts in many modern consumer products. TiO_2 NPs are typically non-toxic when applied to the skin or ingested. We study the effects of inhalation through their interaction with human lung cells (A549).



Cellular Internalization

- **Identify TiO_2 nanoparticle-containing vesicles in A549 cells**

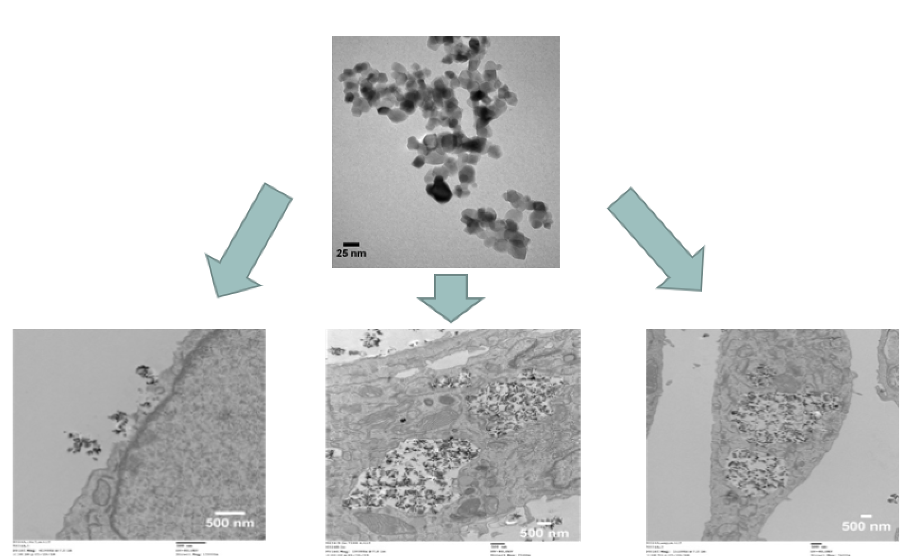


Figure 1: Transmission electron microscopy (TEM) image of TiO_2 NP-containing vesicles

Acknowledgments

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- **Lysosomal Enlargement with NPs**

The A549 cells containing TiO_2 NPs are viewed and examined using fluorescent microscopy methods.

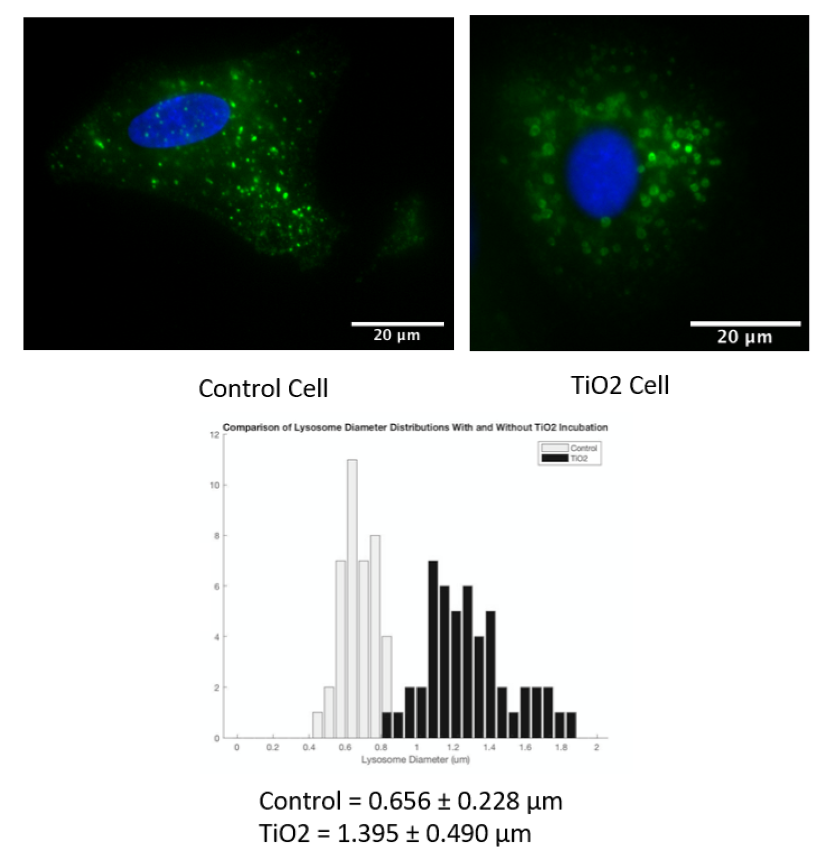

Figure 2: TiO_2 NPs localized in enlarged lysosomes

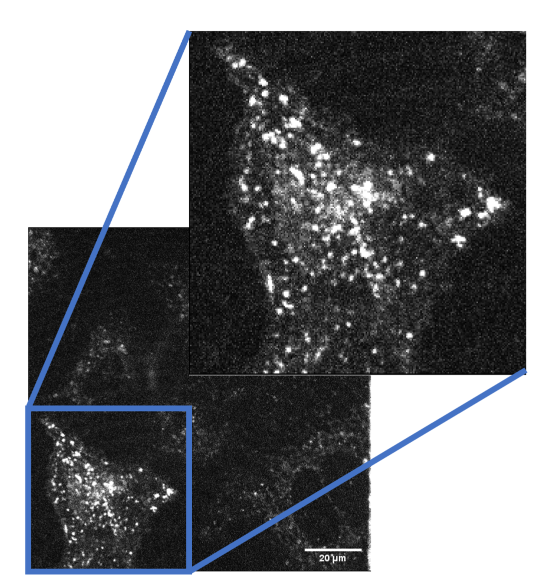

Figure 3: Lysosomes not containing TiO_2 NPs, observed at 1 Hz

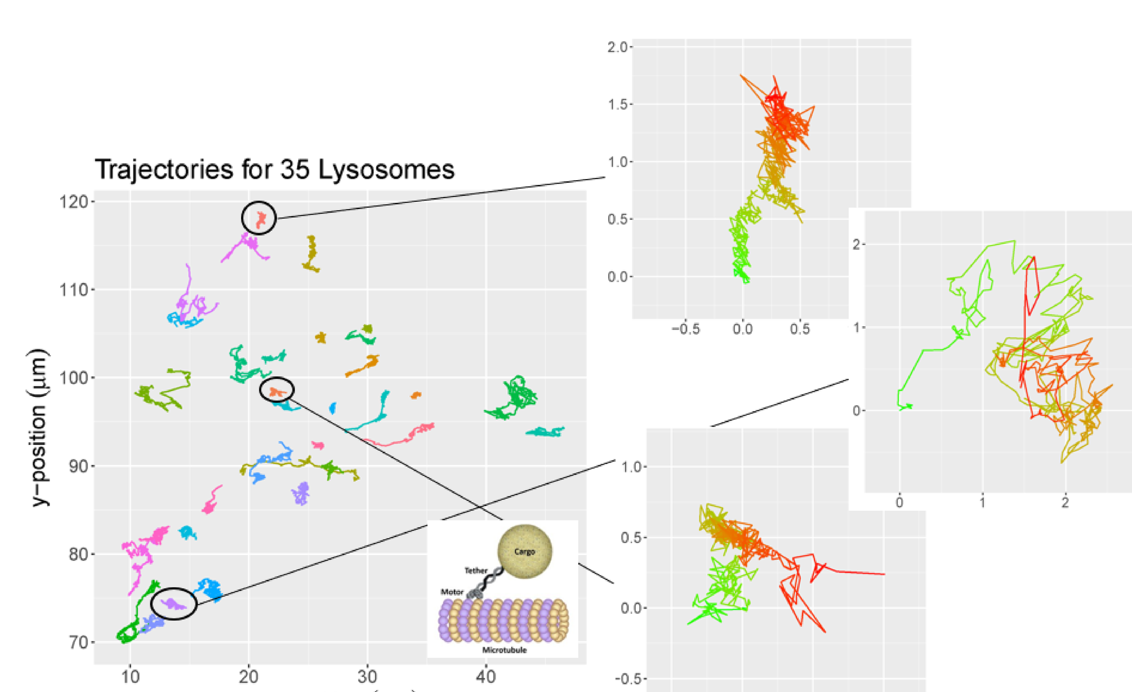

Figure 4: Reconfigured trajectories via R

Single Particle Tracking Analysis

Biophysical Model: We use deterministic equations with additive noise to simulate the x and y positions of the cargo.

$$x_n = u_1(t_{n-1} - \frac{1}{\hat{k}}) + z_0 + N\left(0, \frac{D}{\hat{k}}\right) \quad \text{and} \quad y_n = u_2(t_{n-1} - \frac{1}{\hat{k}}) + z_0 + N\left(0, \frac{D}{\hat{k}}\right)$$

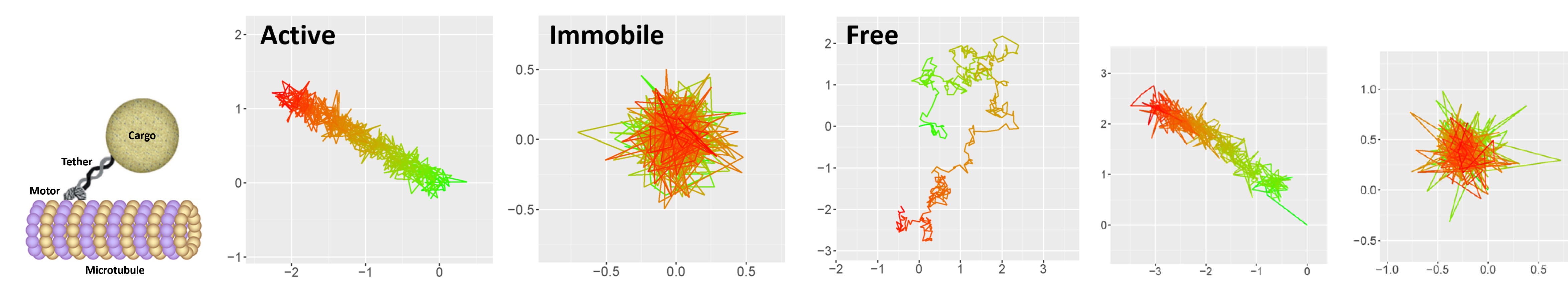

Figure 5: Simulated trajectories of Active, Immobile, and Free transport along a microtubule, each with 500 observations. Trajectories of lysosomes in A549 cells containing TiO_2 NPs captured at 20Hz, each with about 600 observations. (In microns μm)

Statistical Model: We will use Bayesian inference methods to estimate the velocity of each individual lysosome trajectory.

$$\text{Posterior} \propto \text{Likelihood} \times \text{Prior}$$

Let $\eta = \frac{1}{D}$. Thus, we define the likelihood of the next observation given the parameters by

$$L(x_k; u_1, \hat{k}, \eta, z_0) = \Pi_{k=1}^{n} L(x_k; \bar{\theta}) \quad \text{and} \quad L(y_k; u_2, \hat{k}, \eta, z_0) = \Pi_{k=1}^{n} L(y_k; \bar{\theta})$$

The prior probabilities are defined as the following, where the velocities are improper priors, and η is gamma distributed.

$$\Pi_1(u_1) = 1, \qquad \Pi_2(u_2) = 1, \qquad \text{and} \qquad \Pi_3(\eta) = \frac{b^a}{\Gamma(a)}\eta^{a-1}e^{-b\eta}$$

The simplified joint posterior distribution is defined as

$$L(\bar{x}; \bar{\theta})L(\bar{y}; \bar{\theta})\Pi_1(u_1)\Pi_2(u_2)\Pi_3(\eta) = \left(\frac{\hat{k}}{2\pi}\right)^n \frac{b^a}{\Gamma(a)}\eta^{n+a-1}\exp\left(-\eta\left[b + \frac{\hat{k}A_x}{4}\left((u_1 - \frac{B_x}{A_x})^2 - \frac{B_x^2}{A_x^2} + \frac{C_x}{A_x}\right) + \frac{\hat{k}A_y}{4}\left((u_2 - \frac{B_y}{A_y})^2 - \frac{B_y^2}{A_y^2} + \frac{C_y}{A_y}\right)\right]\right)$$

From this we extract the following posterior distributions.

$$\eta \sim Gamma\left(n + a, b + \frac{\hat{k}A_x}{4}\left((u_1 - \frac{B_x}{A_x})^2 - \frac{B_x^2}{A_x^2} + \frac{C_x}{A_x}\right) + \frac{\hat{k}A_y}{4}\left((u_2 - \frac{B_y}{A_y})^2 - \frac{B_y^2}{A_y^2} + \frac{C_y}{A_y}\right)\right)$$

$$u_1 \sim N\left(\frac{B_x}{A_x}, \frac{2}{\eta\hat{k}A_x}\right) \quad \text{and} \quad u_2 \sim N\left(\frac{B_y}{A_y}, \frac{2}{\eta\hat{k}A_y}\right)$$

For each trajectory, we sample 1000 values from each distribution to estimate the best possible value for each parameter.

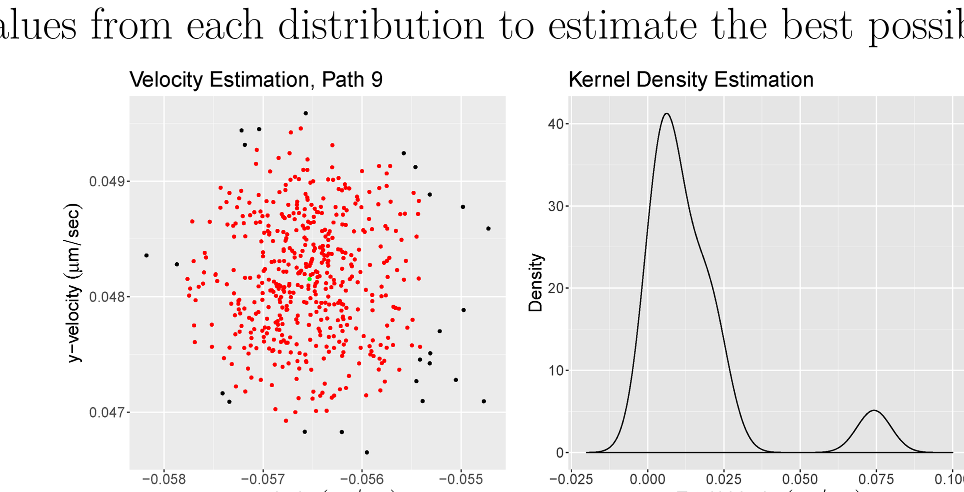

Figure 6: 20Hz frame rate

Future Work

Model selection! Given a path, assign a probability that it is active, immobile, or free based on a score function.