# A pixel-based likelihood framework for analysis of FRAP data

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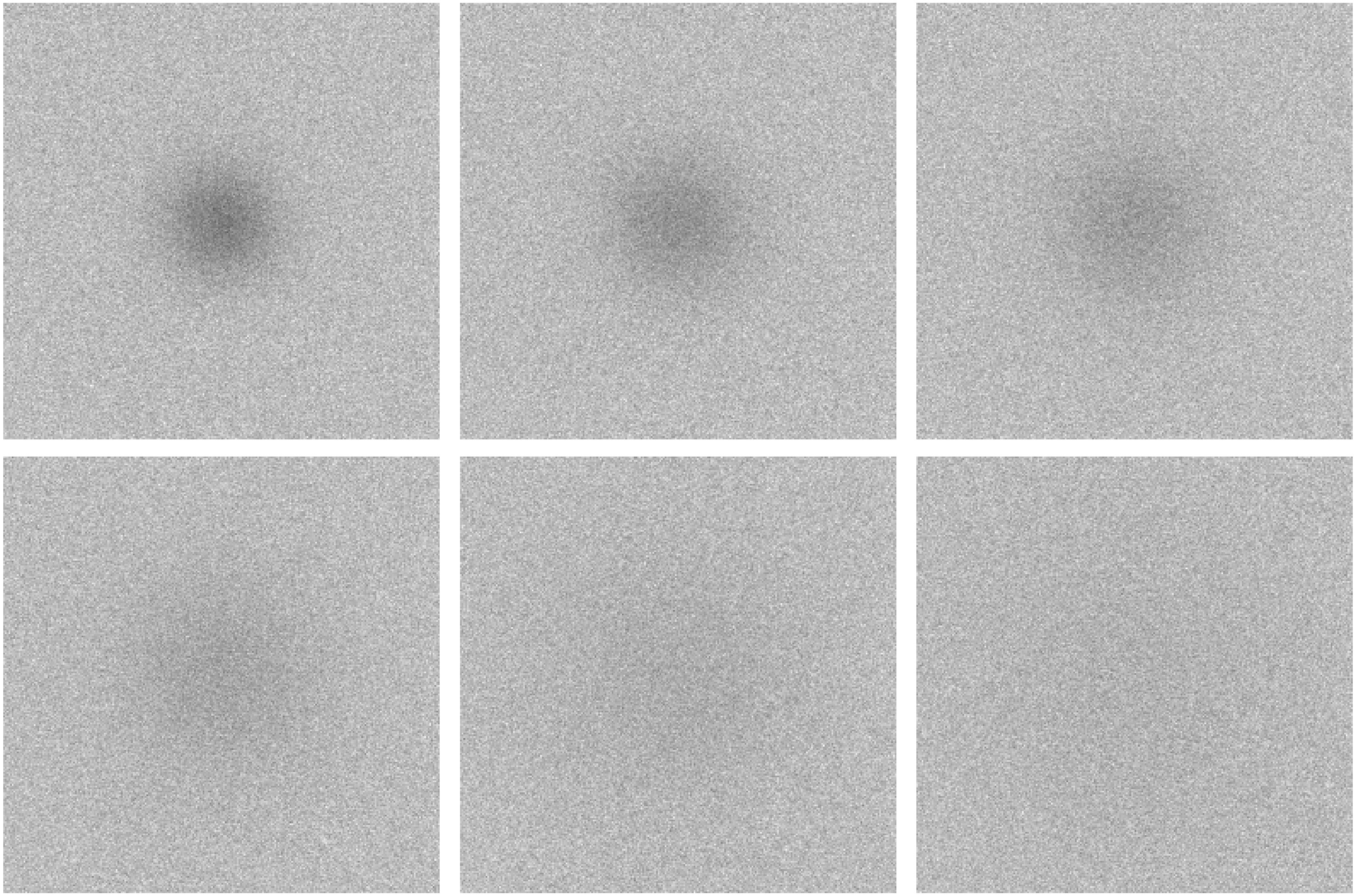
# Images



# Model

Assume rotational symmetry and no diffusion in the $z$-direction. The diffusion equation is

$$\frac{\partial C}{\partial t} = D\left\{\frac{1}{r}\frac{\partial C}{\partial r} + \frac{\partial^2 C}{\partial r^2}\right\}.$$

The solution can be written as

$$C(r,t) = \frac{1}{2Dt}e^{-\frac{r^2}{4Dt}}\int_0^\infty r' C_0(r') I_0\left(\frac{rr'}{2Dt}\right) e^{-\frac{r'^2}{4Dt}}\mathrm{d}r',$$

where $I_0(x) = \frac{1}{\pi}\int_0^\pi \exp(-x\cos t)\mathrm{d}t$ is the modified Bessel function of order zero.

# Model

Using initial concentration,

$$C_o(r) = c_0 - c_1 \exp\left(\frac{-r^2}{r_0^2}\right),$$

the solution of the differential equation is,

$$C(r,t) = c_o - c_1 \frac{r_0^2}{4Dt + r_0^2} \exp\left(\frac{-r^2}{4Dt + r_0^2}\right).$$

$C$ concentration, $D$ diffusion coefficient, $r$ distance from the centre of the bleached disc, $r_0$ radius of the bleached disc.

# Statistical model

- Assume that the pixel value $p(r,t)$ at time $t$ and distance $r$ from the centre of the bleached disc is normally distributed with mean $C(r,t)$ and variance $\sigma^2$.
- Assume that the noise is independent for different pixels.
- The joint likelihood function for all pixels at all times can be written,

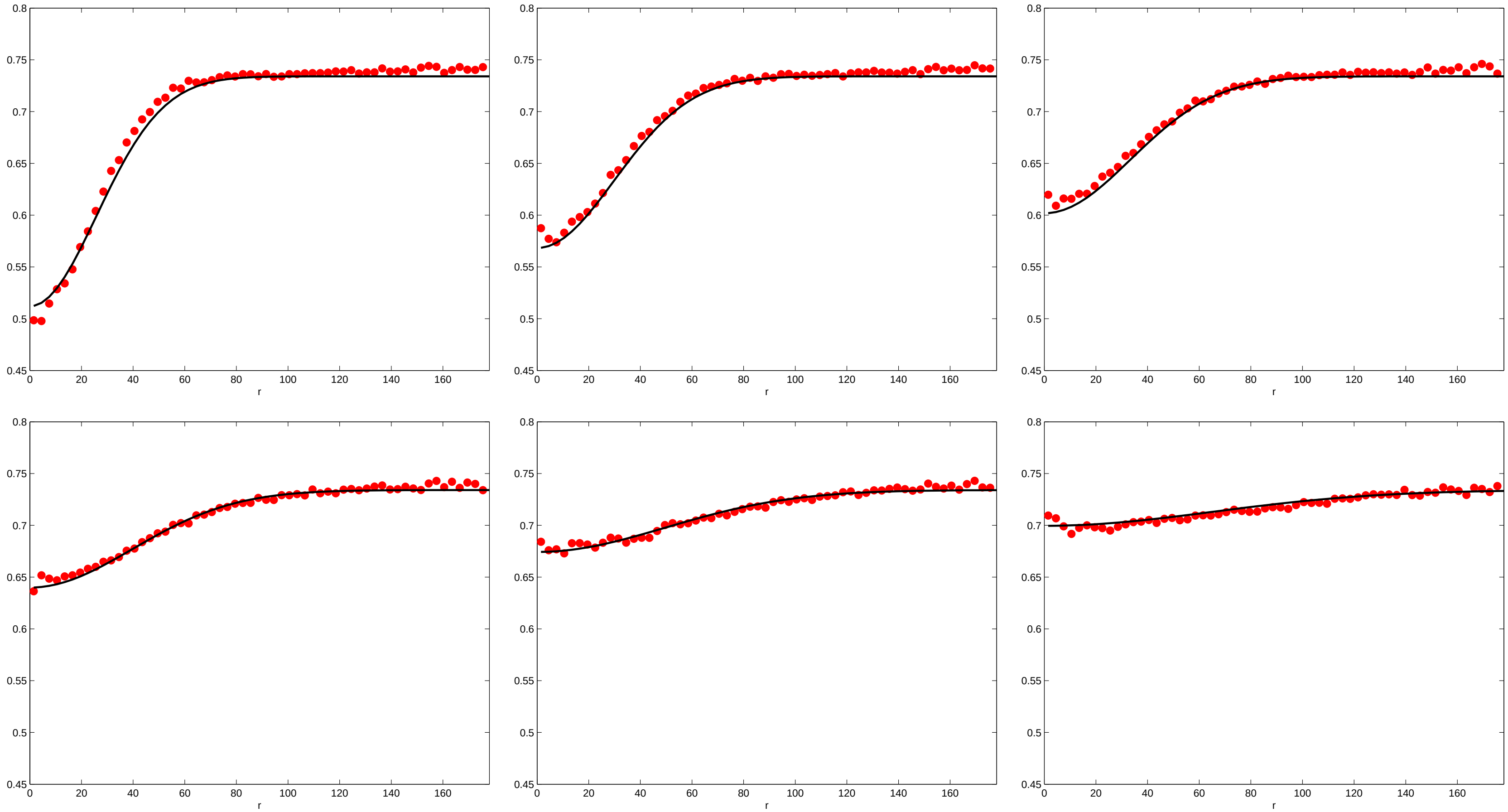
$$\prod_{t\in T}\prod_{i=1}^{N}\frac{1}{\sqrt{2\pi\sigma^2}}\exp\left(-\frac{(p(r_i,t)-C(r_i,t))^2}{2\sigma^2}\right).$$

# Results

- Solution: 25 ppm sodium fluorescein, 20 w/w% polyethylene glycol with average molecular weight 3000 Da and deuterium oxide. (Units in table: $\mu$m$^2$/s)

| Repl. | No pixels | $D$ | s | $\bar{D}$ | $s_{repl}$ | $D$ (NMR) |
|---|---|---|---|---|---|---|
| 1 | 128x128 | 63.5 | 0.8 | | | |
| 2 | 128x128 | 58.9 | 0.8 | | | |
| 3 | 128x128 | 61.4 | 0.8 | | | |
| 4 | 128x128 | 59.8 | 0.8 | 60.9 | 2.0 | 62.0 |
| 1 | 256x256 | 60.9 | 0.4 | | | |
| 2 | 256x256 | 61.9 | 0.4 | | | |
| 3 | 256x256 | 60.2 | 0.4 | | | |
| 4 | 256x256 | 63.0 | 0.5 | 61.5 | 1.2 | 62.0 |

# Fit



# New model

Change initial concentration profile from Gaussian to

- $$g_0(y) = \begin{cases} a_0 - a_1 & y \leq r_0 \\ a_0 & y > r_0. \end{cases}$$

  at time $t_0$ before the first image

or

- estimate an increasing concentration profile from the first image.

Problem: No solution to the differential equation.

# New model

At time $t$ from the inital concentration function the "amount" diffused from a point at distance $d$ can be written

$$f(d,t) = \frac{1}{4\pi Dt} \exp\left(-\frac{d^2}{4Dt}\right)$$

Summing over all pixels

$$\lambda(x,t) = \sum_y g_0(y) f(|x-y|, t+t_0),$$

# New model

- Assume that the pixel value $p(r,t) = kN(x,t)$, where $k$ is a constant and $N(x,t)$ is a Poisson distributed random variable with expectation $\lambda_{x,t}$.
- Assume independence and use the joint likelihood as before.
- Disadvantage: The maximisation of the likelihood is slow if the parametric form is used. With initial concentration estimated from the first image it is possible to maximise the likelihood over $D$ only.

# Future work

- Scanning of the image.
- Models with a mixture of diffusion coefficients.
- Irregularly bleached regions and inhomogeneous media (with additional structure information).
- Variance component estimation.
- Optimal design of series of experiments.