Stimulus-Response Functions

Block, Segall, and Berg, 1982

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Physics 141
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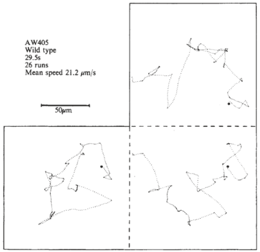
Week 8

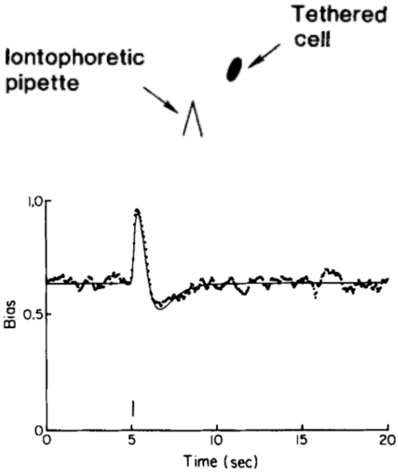
Temporal comparisons in bacterial chemotaxis



Plot of the displacement of a wild-type cell in a homogeneous medium. Runs are exponentially distributed with a mean of about 1 sec. Swimming speed is about 2×10^{-3} cm/s

- The cell is 10^{-4} cm in length.
- The diffusion coefficient of a small molecule is $D = 10^{-5}\text{cm}^2\text{s}^{-1}$
- The time for a molecule to diffuse from one end of a cell to another is ≈ 1 millisecond.
- The cell outruns diffusion when $vt > \sqrt{Dt}$, or roughly one second.

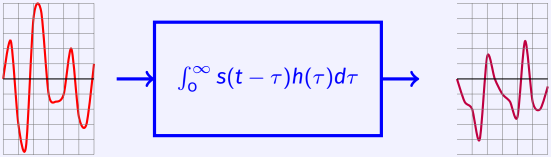
- For rotational diffusion about a single axis, $\langle\theta^2\rangle = 2D_r t$ where $D_r = k_B T/f_r$.
- The rotational frictional drag cofficient of a sphere or radius a is $f_r = 8\pi\eta a^3$
- In 1 sec, a 1 μm sphere diffuses about 30°.
- A cell cannot increase its integration time with longer runs because it “forgets” its direction



- When a cell is exposed to a short impulsive stimulus (pulses of aspartate of small amplitude and width), a biphasic response is obtained.
- The CCW bias rises rapidly, returns to baseline after one second, falls below baseline, and returns to baseline after another 3 seconds
- The impulse response is a weighting function if the system is linear, namely when changes in behavioral response are proportional to changes in stimulus: $\Delta r(t) \propto \Delta s(t)$

Linear response theory

Predicting time-varying response from time-varying stimulus



$s(t)$
stimulus
waveform

Linear
Filter

$r(t)$
response
waveform

- Assume that the response at any given time represents a weighted sum of the values of the stimulus at earlier times

$$r = r_0 + \int_0^\infty d\tau h(\tau)s(t-\tau)$$

- r_0 is the background firing that may occur when $s = 0$.
- $h(t)$ is a weighting factor that determines the sign and strength at which the value of the stimulus at time $t-\tau$ affects the firing rate at time t.

- Functionals map functions to other functions

$$s(t) \mapsto r(t)$$

- The **Volterra expansion** is the functional equivalent of the Taylor series expansion. This generates a power series approximations of functions:

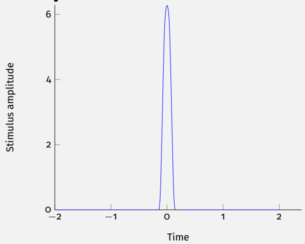
$$\begin{aligned} r(t) = r_0 + \int d\tau D(\tau) s(t-\tau) + \int d\tau_1 d\tau_2 D_2(\tau_1, \tau_2) s(t-\tau_1) s(t-\tau_2) + \\ \int d\tau_1 d\tau_2 d\tau_3 D_3(\tau_1, \tau_2, \tau_3) s(t-\tau_1) s(t-\tau_2) s(t-\tau_3) \dots \end{aligned}$$

- Norbert Wiener rearranged the Volterra expansion. h is called the “first Wiener kernel”, the “linear filter”, or just the “kernel”.

The linear kernel

$$r - r_0 = \int_0^\infty d\tau h(\tau) s(t-\tau)$$

An impulse stimulus



$$s(t) = \frac{1}{(2\pi\sigma^2)^{1/2}} e^{-t^2/2\sigma^2}$$

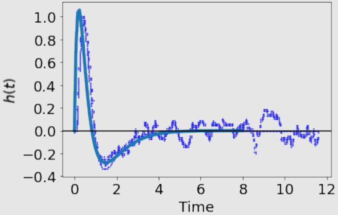
- In the limit that $\sigma \to 0$, the Gaussian function approaches a delta function:

$$\int_{-\infty}^{\infty} f(\tau)\, \underbrace{s(\tau - t)}_{\approx \delta(\tau - t)}\, d\tau \approx f(t)$$

- If the stimulus is sharply peaked at $t = 0$, then the response to the stimulus reflects the value of the kernel at one point:

$$\begin{aligned} r - r_0 &\propto \int_0^\infty d\tau\, h(\tau) \delta(t-\tau) \\ &\propto h(t) \end{aligned}$$

when $s(t) \propto \delta(t)$.



- Fit to sum of four exponentials:

$$h(t) = A\left[\exp\left(-\frac{t}{a}\right) - \exp\left(-\frac{t}{b}\right)\right] + B\left[\exp\left(-\frac{t}{c}\right) - \exp\left(-\frac{t}{d}\right)\right]$$

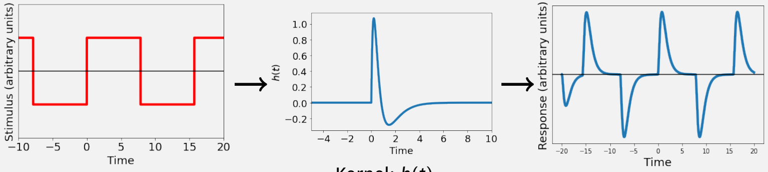
- Area of positive lobe equals area of negative lobe

$$\int_0^\infty h(t)dt = 0$$

- The impulse response positively weights the most recent 1 second of any stimulus waveform and negatively weights the preceding 3 seconds.

$$r(t) \approx s(t-1) - s(t-3)$$

Thus, $r(t) \approx ds/dt$



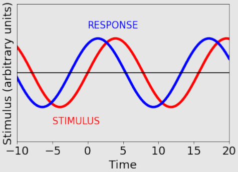
Stimulus waveform: $s(t)$ → Kernel: $h(t)$ → Response waveform: $r(t)$

$$r(t) = \int_0^\infty d\tau h(\tau)s(t-\tau)$$

Any periodic stimulus can be written as a Fourier series:

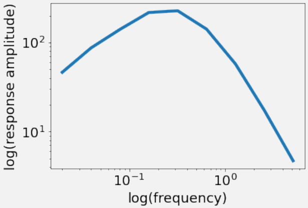
$$s(t) = \sum_{n=-\infty}^{\infty} \hat{s}(\nu_n) e^{-2\pi i (n/T) t} = \frac{a_0}{2} + \sum_{n=1}^{\infty} \left[a_n \cos\left(\frac{2\pi n t}{T}\right) + b_n \sin\left(\frac{2\pi n t}{T}\right) \right]$$

- Decompose a stimulus into sine and cosine waves
- compute the linear mapping of each sine and cosine wave to a response
- reassemble the total response from the original Fourier coefficients



Our linear filter roughly differentiates a sinusoidal stimulus...

... and behaves like a bandpass filter



We want to estimate the linear kernel $h(t)$ that best predicts the system's responses to stimuli:

$$r(t) - r_0 = \int_0^\infty d\tau h(\tau)s(t-\tau).$$

For a specific pair of response and stimulus waveforms, the best guess for the linear kernel minimizes the error or *mean square deviation* between the predicted response $r_{est}(t)$ and the true response:

$$\begin{aligned} E &= \frac{1}{T}\int_0^T dt\,[r_{est}(t) - r(t)]^2 \\ &= \frac{1}{T}\int_0^T dt\left[\left(r_0 + \int_0^\infty d\tau\, h(\tau)s(t-\tau)\right) - r(t)\right]^2 \end{aligned}$$

Finding the function that minimizes an integral can involve the **calculus of variations**.

Approximate the integral as a sum in discrete time steps Δt:

$$E = \frac{1}{N}\sum_{i=0}^{N}\left(r_0 + \Delta t\sum_{k=0}^{\infty} h_k s_{i-k} - r_i\right)^2$$

where $T = N\Delta t$ and

- $r_n = r(n\Delta t)$
- $h_n = h(n\Delta t)$
- $s_n = s(n\Delta t)$

Take the derivative with respect to the value of the kernel at the jth time step, and set it to zero:

$$\frac{\partial E}{\partial h_j} = \frac{2}{N}\sum_{i=0}^{N}\left(r_0 + \Delta t\sum_{k=0}^{\infty} h_k s_{i-k} - r_i\right) s_{i-j}\Delta t = 0$$

After rearrangement

$$\Delta t \sum_{k=0}^{\infty} h_k \left(\frac{1}{N} \sum_{i=0}^{N} s_{i-k} s_{i-j} \right) = \frac{1}{N} \sum_{i=0}^{N} (r_i - r_0) s_{i-j} \tag{1}$$

Turn the sums back into integrals

- $i\Delta t \to t$
- $j\Delta t \to \tau$
- $k\Delta t \to \tau'$
- and take limit $\Delta t \to 0$

$$\int_0^{\infty} d\tau' h(\tau') \left(\frac{1}{T} \int_0^T dt\, s(t-\tau') s(t-\tau) \right) = \frac{1}{T} \int_0^T dt\, (r(t) - r_0) s(t-\tau)$$

Simplify using the definitions of correlation functions

- $R_{rs} = (r \star s)(-\tau) = \int_0^T dt\, r(t)s(t-\tau)$
- $R_{ss} = (s \star s)(\tau - \tau') = \int_0^T dt\, s(t)s(t+\tau-\tau')$

$$\int_{-\infty}^{\infty} d\tau' R_{ss}(\tau - \tau')h(\tau') = R_{rs}(-\tau)$$

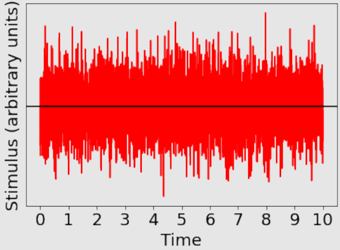
The Fourier Transform

$$\hat{f}(\nu) = \int_{-\infty}^{+\infty} dt f(t) \exp -2\pi i \nu t$$

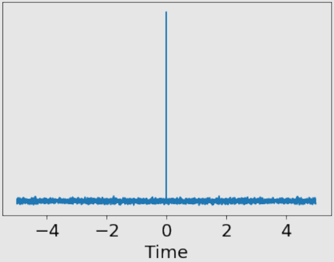
$$f(t) = \int_{-\infty}^{+\infty} d\omega \tilde{D}(\omega) \exp(2\pi)$$

- For white noise, $Q_{ss}(\tau) = \sigma^2\delta(\tau)$
- Hence, the kernel is proportional to the correlation between stimulus and response evaluated at $-\tau$:

$$D(\tau) = \frac{Q_{rs}(-\tau)}{\sigma_s^2} \tag{2}$$



White Noise



Q_{ss}

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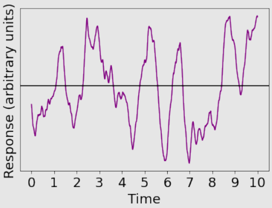
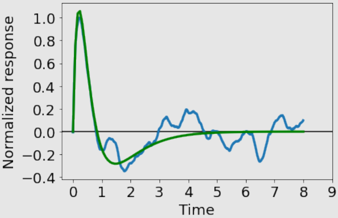


Response to white noise:
$r(t) = \int_0^\infty D(\tau)s(t-\tau)d\tau$



$Q_{rs}(-t)$.
$D(t)$.