Biophysical modeling

In principle information may be encoded at any lengthscale or timescale, including at the molecular level, e.g., at the synaptic cleft (number of ion channels, metabotropic receptors may encode ≠ states of the synapse).

Question: Can we give simple estimate for information transfer at such microscopic level? Can infer some design principle via optimization principles?

Simple case: encoding via leaky integration of molecules.

$A \longrightarrow M$

A: driving signal

M: molecular counts → typically ≥ 100 → high molecular counts justifies diffusive approx.

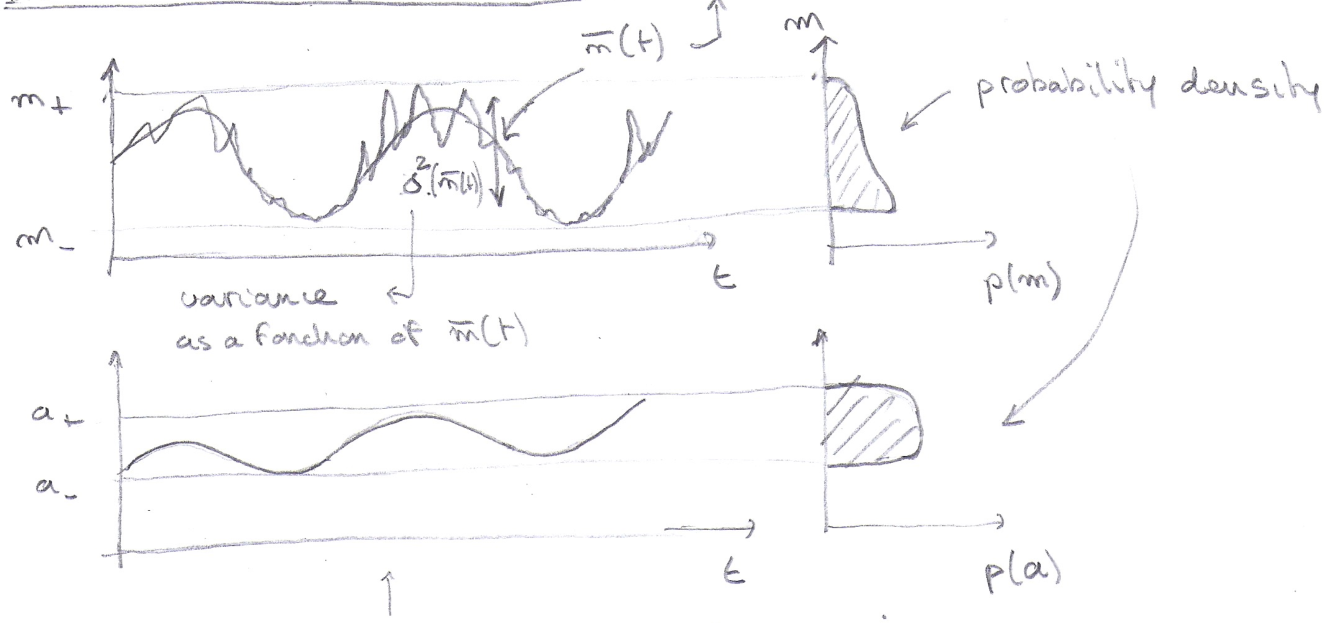
↓

biophysical model for information channel:

$$\dot{m}_t = \Big(\underbrace{f(a_t)}_{\text{input dependent production rate}} - \underbrace{\frac{m_t}{\tau}}_{\text{degradation leak rate}}\Big) + \underbrace{\sqrt{f(a_t) + \frac{m_t}{\tau}}}_{\text{noise amplitude deduced from Poisson statistics}}\ \xi_t$$

ξ_t ← Gaussian white noise

Quasistatic approximation



external drive is slowly varying : $\tau_a \ll \tau$

Small-noise approximation: $\sigma(\overline{m}(t)) \ll \overline{m}(t)$

↳ justify Gaussian approximation of Poisson statistics

Biophysical constraints: Finite range of variation

(a_-, a_+) and (m_-, m_+)

Gaussian information channel: specified by

a mean input/output function $\overline{m}(a)$ and a noise function $\sigma(\overline{m})$ that can be experimentally estimated

Information transfer

$$I(A,M) = H(M) - H(M|A) \leftarrow \text{mutual information}$$

Gaussian channel $\rightarrow H(M|A=a) = \log\left(\sqrt{2\pi e}\,\sigma(\bar{m}(a))\right)$

Small-noise approx $\rightarrow p(m) = \dfrac{p(a)}{\bar{m}'(a)}$: "localization of the output entropy"

approx

$$\tilde{I}(A,M) = \overbrace{-\int da\, p(a) \log \frac{p(a)}{\bar{m}'(a)}}^{H(M)} - \int da\, p(a) \log\left(\sqrt{2\pi e}\,\sigma(\bar{m}(a))\right)$$

$$= H(A) + \int_{a_-}^{a_+} da\, p(a) \log\left(\frac{\bar{m}'(a)}{\sqrt{2\pi e}\,\sigma(\bar{m}(a))}\right)$$

Optimal information transfer

Variable of optimization = rate of production $f \longleftrightarrow \bar{m}$

$\bar{m}$ and σ are obtained by linearization:

(*) $\bar{m} = \tau f(a)$ (**) $\dot{\delta m_t} = \dfrac{\delta m_t}{\tau} + \underbrace{\sqrt{f(a) + \frac{\bar{m}}{\tau}}}_{\sqrt{\frac{2}{\tau}}\sqrt{\bar{m}}}\, \xi_t$

$\delta m_t = m_t - \bar{m}$

$$\sigma^2(m) = \mathbb{E}[\delta m^2] = \frac{2/\tau\, \bar{m}}{2(1/\tau)} = \bar{m} \leftarrow \text{Poisson noise model}$$

More general model consider $\sigma(\bar{m})$ as an arbitrary positive function

$$\dot{\delta m_t} = \frac{\delta m_t}{\tau} + \sqrt{\frac{2}{\tau}}\,\sigma(\bar{m})\,\xi_t$$

at fixed $\bar{m} = \bar{m}(a)$

Problem in the calculus of variation

$$\hat{I}(A,M) = \underset{\substack{\uparrow \\ \text{Fixed}}}{H(A)} + \int_{a_-}^{a_+} da\; p(a) \log\left(\frac{\bar{S}'(a)}{\sqrt{2\pi e}}\right) \longrightarrow \underset{\substack{\shortparallel \\ \text{Lagrangian}}}{L[\bar{S}', \bar{S}, a]}$$

$$\bar{S}(a) = S(\bar{m}(a)), \qquad S(m) = \int_{m_-}^{m} \frac{dm'}{\sigma(m')}$$

Euler-Lagrange equation: $\quad \frac{\partial L}{\partial \bar{S}} - \frac{\partial}{\partial a}\left[\frac{\partial L}{\partial \bar{S}'}\right] = 0$

$$\frac{\partial}{\partial a}\left[\frac{p(a)}{\bar{S}'(a)}\right] = 0 \implies \bar{S}'(a) = \underset{\substack{\uparrow \\ \text{unknown constant}}}{Z}\; p(a)$$

but $Z = Z \int_{a_-}^{a_+} p(a)\,da = \bar{S}(a_+) - \bar{S}(a_-) = \int_{m_-}^{m_+} \frac{dm'}{\sigma(m')}$

moreover the stationary input-output function satisfies

$$S(\bar{m}(a)) - S(m_-) = Z \int_{a_-}^{a} p(a')\,da' = Z\, C(a) \leftarrow \text{cumulative}$$

$$\bar{m}(a) = S^{-1}\Big(S(m_-) - \underbrace{\big(S(m_+) - S(m_-)\big)}_{Z}\, P(a)\Big)$$

One can check that this corresponds to the maximum of $\tilde{I}(A,M)$:

$$\boxed{\begin{aligned} \tilde{I}^*(A,M) = \max_F \tilde{I}(A,M) &= \cancel{H(A)} + \int_{a_-}^{a_+} da\, p(a) \log\left(Z\, \cancel{p(a)} / \sqrt{2\pi e}\right) \\ &= \left(\int_{a_-}^{a_+} da\, p(a)\right) \log Z/\sqrt{2\pi e} = \log\left(\frac{1}{\sqrt{2\pi e}} \int_{m_-}^{m_+} \frac{dm}{\sigma(m')}\right) \end{aligned}}$$

⚠ does not depend on inputs = it is the small-noise capacity too!

Interpretation

In the small noise approximation, varying the input distribution is equivalent to a change of variable: $p(m) = \dfrac{p(a)}{\bar{m}'(a)}$.

Histogram equalization with inhomogeneous noise:

$$p(m) = p(\cancel{a}) \Big/ \Big(Z\, p(\cancel{a}) \Big/ S'\big(\overbrace{S(m_-) + Z\, C(a)}^{m}\big)\Big) \; ;$$

$$p(m) = \frac{S'(m)}{Z} = \frac{1}{\int_{m_-}^{m_+} dm/\sigma(m)} \qquad 1/\sigma(m)$$

↳ output word should be used inversely proportionally to the associated noise level.

Information role of Feedback

In theory, there is no benefit of feedback for promoting information transfer. In a biophysical context however one can define an information role for feedback.

Feedback model

effective noise model

$$\dot{m}_t = \left(f(a_t)\, g(m_t) - \frac{m_t}{\tau} \right) + \sqrt{2}\, \sigma(m_t)\, \xi_t$$

Fast feedback: modulation of the production rate

$$\begin{tikzcd} A \arrow[r] & M \arrow[loop right] \end{tikzcd} \qquad m_- = f_- g_- \qquad m_+ = f_+ g_+$$

Gaussian channel

boundary conditions

Linearization

differentiation w.r.t a

$$(*) \quad \tau f(a)\, g(\bar{m}) = \bar{m} \;\Rightarrow\; \tau\left(f'(a)\, g(\bar{m}) + f(a)\, g'(\bar{m}) \right) = \bar{m}'$$

$$(**) \quad \delta \dot{m}_t = -\left(\frac{1}{\tau} - f(a)\, g'(\bar{m}) \right) \delta m_t + \sqrt{\frac{2}{\tau}}\, \sigma(\bar{m})\, \xi_t$$

$$\Sigma^2(\bar{m}) = \frac{2/\tau\, \sigma^2(\bar{m})}{2\left(1/\tau - f(a)\, g'(\bar{m})\right)} \underset{(*)}{=} \frac{\sigma^2(\bar{m})}{\tau f'(a)\, g(\bar{m})}$$

Optimization over production rate f and feedback g

$$I(A,M) = H(A) + \frac{1}{2} \int_{a_-}^{a_+} da\, p(a) \log\left(\frac{\bar{m}'(a)^2}{2\pi e\, \Sigma^2(\bar{m}(a))} \right) \qquad (*)\ \frac{\bar{m}}{\tau f(a)}$$

$$= H(A) + \frac{1}{2} \int_{a_-}^{a_+} da\, p(a) \log\left(\frac{\bar{m}'(a)^{\cancel{2}}\, \tau f'(a)\, g(\bar{m}(a))}{2\pi e\, \sigma^2(\bar{m}(a))\, \cancel{\bar{m}'(a)}} \right)$$

$$= H(A) + \frac{1}{2} \left[\int_{a_-}^{a_+} da\, p(a) \log\left(\frac{f'(a)}{f(a)} \right) + \int_{a_-}^{a_+} da\, p(a) \log\left(\frac{\bar{m}'(a)\, \bar{m}(a)}{\sigma^2(\bar{m}(a))} \right) \right]$$

independent optimization

$$F(m) = \int_{m_-}^{m} \frac{m}{\sigma^2(m)}\, dm$$

Calculus resolution

- $F'(a)/F(a) = Z_F\, p(a)$
- $Z_F = \ln\left(F_+/F_-\right)$
- $F(a) = F_-\left(F_+/F_-\right)^{C(a)}$
- $p(F) = \dfrac{1}{\ln\left(F_+/F_-\right)} \dfrac{1}{F}$

- $\dfrac{\bar{m}'(a)\,\bar{m}(a)}{\sigma^2(\bar{m}(a))} = Z_m\, p(a)$
- $Z_m = \int_{m_-}^{m_+} m/\sigma^2(m)\, dm = F(m_+) - F(m_-)$
- $\bar{m}(a) = F^{-1}\left(F(m_-) + (F(m_+) - F(m_-))P(a)\right)$
- $p(m) = \dfrac{1}{\int_{m_-}^{m_+} \frac{m\,dm}{\sigma(m)}} \dfrac{m}{\sigma^2(m)}$

Fano factor

Information gain

$$\tilde{I}^*(A,M) = \cancel{H(A)} - \frac{1}{2}\left(\cancel{H(A)} + \cancel{H(A)}\right) + \underbrace{\int_{a_-}^{a_+} da\, p(a)}_{=1} \log\left(\ln F_+/F_- \int_{m_-}^{m_+} \frac{m}{\sigma^2(m)}\, dm\right)$$

capacity !

$$\Delta I(A,M) = \tilde{I}^*(A,M) - \tilde{I}^*_\phi(A,M) \leftarrow \text{no feedback}$$

$$= \log\left(\ln\left(F_+/F_-\right) \int_{m_-}^{m_+} \frac{m}{\sigma^2(m)}\, dm \Big/ \int_{m_-}^{m_+} dm/\sigma(m)\right)$$

Cauchy-Schwarz: $\int_{m_-}^{m_+} dm/\sigma(m) \leq \int_{m_-}^{m_+} dm/m \int_{m_-}^{m_+} m/\sigma^2(m)\, dm$

$$\leq \log\left(m_+/m_-\right) \int_{m_-}^{m_+} m/\sigma^2(m)\, dm$$

$$\boxed{\Delta I(A,M) \geqslant \log\left(\frac{\ln\left(F_+/F_-\right)}{\ln\left(m_+/m_-\right)}\right)}$$

$\Rightarrow$ negative feedback

$g_+ = m_+/F_+ < 1$

positive feedback

$g_- = m_-/F_- > 1$