Deterministic and Stochastic Models of Bicoid Protein Gradient Formation in Drosophila Embryos

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Drosophila
Morphogen Concentration

Thresholds

Start

Spatial axis

French Flag
Bicoid Morphogen

- Drosophila body plan and position information.
- Providing the concentration mechanism to activate other gap gene in drosophila embryo.
- Contributing to set up the anterior posterior axis.
- Controlling cells fate along 70% of this axis.
Bicoid Morphogen Concentration

Anterior part

Posterior part
Constant Source

- Usual assumption

\[ S_{con}(x, t) = S_0 \delta(x) \Theta(t) \]
New Source Model

\[ S_{com} = S_0 \delta(x)(\Theta(t) - \Theta(t - t_0)) + S_0 \delta(x)\Theta(t - t_0) \exp \left\{ -\frac{t - t_0}{\tau_m} \right\} \]

The reaction-diffusion equation of single-morphogen concentration system is below:

\[
\frac{\partial}{\partial t} M(x,t) = D \frac{\partial^2}{\partial x^2} M(x,t) - \tau_p^{-1} M(x,t) + S(x,t)
\]

- \(M(x,t)\) is morphogen concentration
- \(S(x,t)\) is a general source term at the anterior pole
- \(D\) is diffusion constant
- \(\tau_p\) is half-life of the morphogen protein

Turing, A.: *The chemical basis of morphogenesis.* (1952)
Bergmann, S.: *Pre-Steady-State Decoding of the Bicoid Morphogen Gradient.* (2007)
The reaction-diffusion equation of single-morphogen concentration system with cytoplasmic flow:

\[
\frac{\partial}{\partial t} M(x,t) = D \frac{\partial^2}{\partial x^2} M(x,t) - \tau_p^{-1} M(x,t) - v \frac{\partial}{\partial x} M(x,t) + S(x,t)
\]

- \(M(x,t)\) is morphogen concentration
- \(S(x,t)\) is a general source term at the anterior pole
- \(D\) is diffusion constant
- \(\tau_p\) is half-life of the morphogen protein
- \(v\) is flow velocity

Hecht, I. : *Determining the scale of the Bicoid morphogen gradient*. (2009)
Stochastic Model

- Bicoid proteins chemical reaction diffusion

... 100 subvolumes ...

\[ S(t) \]

- Bicoid proteins production

- Bicoid proteins degradation

- Bicoid proteins diffusion
Solution to Model with Constant Source

![Diagram showing the solution to the model with constant source, with axes labeled for time (t), position (x), and production rate (S_{con})]
Solution to Model with Combined Source
Solution to Stochastic model
Measured Data

- Integrated 2D patterns - reconstructed image 14A-2

![Graph showing integrated 2D patterns with reconstructed image 14A-2]
Measured Data

- 1D integrated data - cycle 14A (1-8 classes)
Matching Models to Data

Diffusion model with realistic source

Flyex Database

Time (mins)
Comparison Between Model Output and Database in Cycle14A with 8 Classes
Comparison Between Model Output and Database in Cycle14A with 8 Classes
Estimating Parameter Values

- Squared error between model output and measured intensities to evaluate error.

\[ E = \sum_{t=T_1}^{T_2} \sum_{x=1}^{L} \left( M(x,t) - M_d(x,t) \right)^2 \]

- Parameters estimation:
  - Diffusion constant \( D = 1.8 \mu m^2 / s \),
  - The time mRNA starts to decay \( t_0 = 118 \) mins,
  - mRNA half-life \( \tau_m = 29 \) mins
  - Bicoid protein half-life \( \tau_p = 120 \) mins.
Matching Parameter Values to Data

- The errors in the joint space of diffusion constant and maternal mRNA decay onset time.
Conclusion

- Widely used model with a constant source is unrealistic.
- Three models with realistic source.
- Matching models output to database.
- Developing data driven model for embryo spatio-temporal data i.e. Kriged Kalman Filter
Dynamic control of positional information in the early *Drosophila* embryo

Johannes Jaeger, Svetlana Surkova, Maxim Blagov, Hilde Janssens, David Kosman, Konstantin N. Kozlov, Manu, Ekaterina Myasnikova, Carlos E. Vanario-Alonso, Maria Samsonova, David H. Sharp & John Reinitz