

Model inference from protein time-course in Hematopoietic Stem Cells (HSC)

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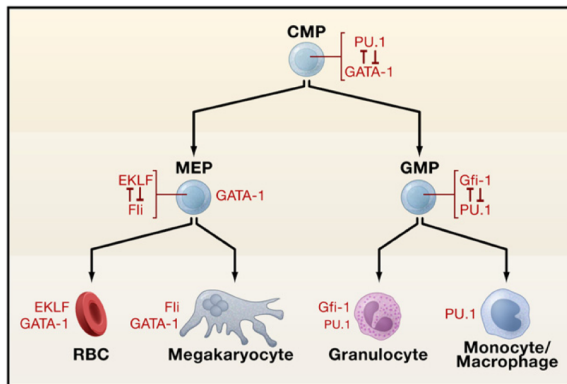
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Introduction

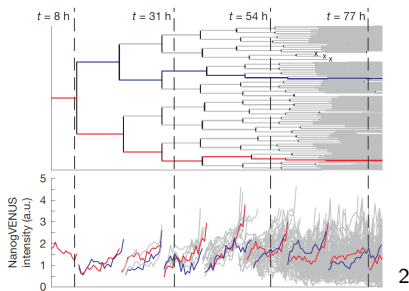
- Dynamics of hematopoietic stem cell maturation cell from Common Myeloid Progenitor (CMP) to Megakaryocyte-Erythroid Progenitor (MEP) and Granulocyte-Macrophage Progenitor (GMP)



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Introduction (cont'd)

- ▶ MEP and GMP yield not 50% : 50% as previously thought, but 70% : 30%
- ▶ Assumed dynamics between Pu.1 and Gata1 in cell maturation fate
 - ▶ Dynamics assumed to be a bistable toggle-switch system
- ▶ Analysis on single-cell time-lapsed data



Problems

- ▶ Stochasticity in single cell resolution is more punctuated
- ▶ Tree structure of the data add ore complexity: inheritance of information during inference process is not trivial

Ideas

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- ▶ **problem:** Overfitting due to single-cell biased
- ▶ **solution:** Inference across cell lineages
- ▶ Inferred parameters from all simulated lineages are represented as distribution
- ▶ Final inferred parameters are expected value E of the distribution

Particle Filtering (6)

Particle Filtering (7)

Particle Filtering: algorithm

1. Initialization of parameters θ .
2. Input of data \mathcal{D} .
3. Particle filtering routine:

3.1 Generation of initial particles for step i

$$K_i := (K_{i1}, K_{i2}, \dots, K_{im}) \quad (1)$$

3.2 Simulation run of each particle K_{ij}

3.3 Weighting of each particle. The weight is a function of the probability of observing the data given the simulation result.

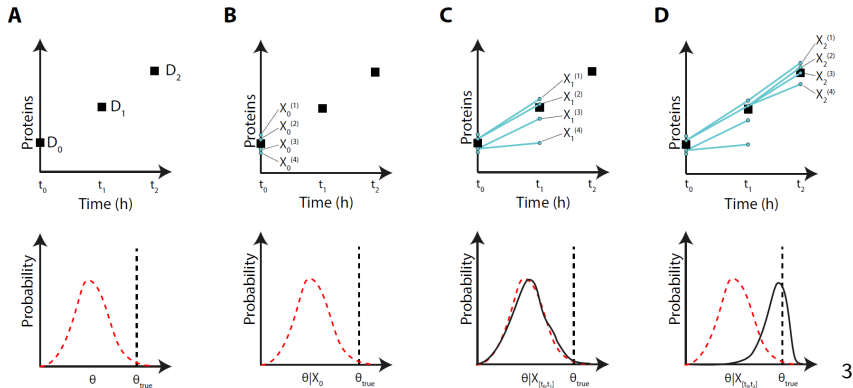
$$w_i^k = P(D_i | X_i^k) = \mathcal{N}(\mathcal{D}_i | X_i^k) \quad (2)$$

3.4 Parameter update for every K,

$$\theta^k \propto P(\theta | X_{[t_0, t_i]}^k) \quad (3)$$

4. Model comparison.

Particle Filtering: visualization



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