Coupled enhancer-promoter condensates

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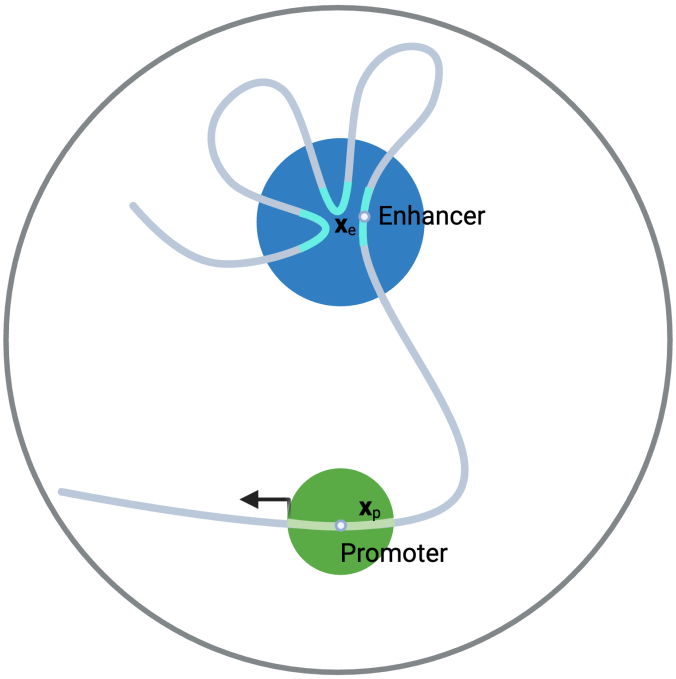

Figure 1: Enhancer and promoter regions on chromatin

1 Free energy functional

$$
\begin{aligned}
F(\phi_{\mathrm{P}}(\vec{x},t),\phi_{\mathrm{R}}(\vec{x},t)) = \int \mathrm{d}\vec{x} & \rho_{\mathrm{P}}(\phi_{\mathrm{P}}-\alpha)^2(\phi_{\mathrm{P}}-\beta)^2 \\
& + \rho_{\mathrm{R}}\phi_{\mathrm{R}}^2 \\
& - \chi\phi_{\mathrm{P}}\phi_{\mathrm{R}} + c\phi_{\mathrm{P}}^2\phi_{\mathrm{R}}^2 \\
& + \frac{\kappa}{2}|\nabla\phi_{\mathrm{P}}|^2 \\
& - \chi_{\mathrm{PD}}\phi_{\mathrm{P}} \exp\left\{-\frac{(\vec{x}-\vec{x_e})^2}{2\sigma^2}\right\} \\
& + F_C
\end{aligned}
$$

- Protein-protein double-well potential

$$F_{\mathrm{DW}} = \rho_{\mathrm{P}}(\phi_{\mathrm{P}}-\alpha)^2(\phi_{\mathrm{P}}-\beta)^2$$

- RNA-RNA repulsion

$$\rho_{\mathrm{R}}\phi_{\mathrm{R}}^2$$

- Protein-RNA electrostatic interaction

$$\chi_{\mathrm{PR}}(\phi_{\mathrm{P}},\phi_{\mathrm{R}}) = \chi\phi_{\mathrm{P}}\phi_{\mathrm{R}} + c\phi_{\mathrm{P}}^2\phi_{\mathrm{R}}^2$$

- Protein-DNA interaction

$$\chi_{\mathrm{PD}}\phi_{\mathrm{P}}\phi_{\mathrm{D}} = \chi_{\mathrm{PD}}\phi_{\mathrm{P}} \exp\left\{-\frac{(\vec{x}-\vec{x_e})^2}{2\sigma^2}\right\}$$

- Interfacial surface-tension

$$\frac{\kappa}{2}|\nabla\phi_{\mathrm{P}}|^2$$

- Chromatin
  - Double-stranded DNA $L_P \approx 50$ nm (Bustamante et al. 1994), not chromatin with nucleosomes.
  - From base pair distanceL_C can be 10^6 nm (Krivega and Dean 2012), not chromatin with nucleosomes.
  - $\vec{R}$ can be 300 to 1000 nm (Cho et al. 2018).
  - Worm-like chain for $L_C \approx L_P$ and $L_C > L_P$
  - Harmonic potential for small deformations

$$F_{\mathrm{C}} = \frac{1}{2}k(|\vec{R}|-L_C)^2 = \frac{1}{2}k(|\vec{x}_{\mathrm{e}}-\vec{x}_{\mathrm{p}}|-L_C)^2$$

  - Gaussian chain for $L_C \gg L_P$ Using $l = L_P$ and $N = L_C/L_P$

$$F(\vec{R}) = \frac{3k_BT}{2}\left(\frac{|\vec{R}|^2}{L_CL_P}\right)$$

2 Dynamic equations

- Protein dynamics Model A dynamics. The amount of protein is conserved.

$$\frac{\partial \phi_{\mathrm{P}}}{\partial t} = M_{\mathrm{P}} \nabla^2 \left(\frac{\partial F}{\partial \phi_{\mathrm{P}}} \right) = M_{\mathrm{P}} \nabla^2 \mu_{\mathrm{P}}$$

- RNA dynamics

$$\frac{\partial \phi_{\mathrm{R}}}{\partial t} = M_{\mathrm{R}} \nabla^2 \phi_{\mathrm{R}} + k_p(\vec{x}) \phi_{\mathrm{P}} - k_d \phi_{\mathrm{R}}$$

$$k_p(\vec{x}) = \frac{k_T}{2\pi\sigma^2} \exp\left\{ \frac{(\vec{x} - \vec{x_p})^2}{2\sigma^2} \right\}$$

- Enhancer region dynamics
  - Gradient of free energy functional with respect to the vector $\vec{x}_e$

$$\frac{\partial \vec{x}_{\mathrm{e}}}{\partial t} = M_{\mathrm{D}} \nabla_{\vec{x}_e} F$$

Bustamante, C., J. F. Marko, E. D. Siggia, and S. Smith. 1994. "Entropic Elasticity of λ-Phage DNA." *Science* 265 (5178): 1599–1600. https://doi.org/10.1126/science.8079175.

Cho, Won-Ki, Jan-Hendrik Spille, Micca Hecht, Choongman Lee, Charles Li, Valentin Grube, and Ibrahim I. Cisse. 2018. "Mediator and RNA Polymerase II Clusters Associate in Transcription-Dependent Condensates." *Science* 361 (6400): 412–15. https://doi.org/10.1126/science.aar4199.

Krivega, Ivan, and Ann Dean. 2012. "Enhancer and Promoter Interactions — Long Distance Calls." *Current Opinion in Genetics & Development* 22 (2): 79–85. https://doi.org/10.1016/j.gde.2011.11.001.