Mathematical Modelling of DNA
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Session 12 — R. Sharma, R. Singh

1 Positive Definiteness of the cgDNA+ stiffness matrix and Invariance of the parameter set

Let $\mathcal{P} = \left\{K^{\alpha\beta} \in \mathbb{R}^{42\times 42}, \sigma^{\alpha\beta} \in \mathbb{R}^{42}, K^{5'\alpha\beta} \in \mathbb{R}^{36\times 36}, \sigma^{5'\alpha\beta} \in \mathbb{R}^{36}, K^{\alpha\beta\ 3'} \in \mathbb{R}^{36\times 36}, \sigma^{\alpha\beta\ 3'} \in \mathbb{R}^{36} | \alpha\beta \in D\right\}$ be a cgDNA+ parameter set (recall from lecture of week 7) where D is the set of all dimers (two base pairs) formed using the alphabet $M = \{A, T, C, G\}$, and let $S = X_1, X_2, \ldots, X_N$ be a sequence with $X_i \in \{A, T, C, G\}$. Note that here we are saying that parameter set ($\mathcal{P}$) contains parameters corresponding to $3'$ end ($K^{\alpha\beta\ 3'}$, $\sigma^{\alpha\beta\ 3'}$) and parameters corresponding to $5'$ end ($K^{5'\alpha\beta}, \sigma^{5'\alpha\beta}$) separately. However in the next part of the exercise we will see that both ($5'$ and $3'$ ends) are related by symmetry.

1. Assume that

$$\begin{aligned} K^{\alpha\beta} &> 0, && (1)\\ K^{5'\alpha\beta} &> 0, && (2)\\ K^{\alpha\beta\ 3'} &> 0, && (3) \end{aligned}$$

for all $K^{\alpha\beta}$, $K^{5'\alpha\beta}$, and $K^{3'\alpha\beta}$ in $\mathcal{P}$. Show that the cgDNA+ stiffness matrix $K(S, \mathcal{P})$ is positive definite for any sequence S.

2. Define E_N as a block trailing-diagonal matrix with $2N - 1$ copies of E interspersed with $2(N - 1)$ copies of I where $E = diag(-1, 1, 1, -1, 1, 1)$, $I = diag(1, 1, 1, 1, 1, 1)$ and define by $\overline{S}$ the complementary sequence of S. See Qu5 Serie 6 for notation of E_N and for symmetry of coordinates system. By assuming

$$\begin{aligned} K^{\overline{\beta}\overline{\alpha}} &= E^{int} K^{\alpha\beta} E_3,\\ \sigma^{\overline{\beta}\overline{\alpha}} &= E^{int} \sigma^{\alpha\beta},\\ K^{\overline{\beta}\overline{\alpha}\ 3'} &= E^{5'} K^{5'\alpha\beta} E_3,\\ \sigma^{\overline{\beta}\overline{\alpha}\ 3'} &= E^{5'} \sigma^{5'\alpha\beta}, && (4) \end{aligned}$$

where,

$$\mathbb{R}^{42\times 42} \ni E^{int} = \begin{bmatrix} & & & & & & I\\ & & & & & E & \\ & & & & I & & \\ & & & E & & & \\ & & I & & & & \\ & E & & & & & \\ I & & & & & & \end{bmatrix}$$

$$\mathbb{R}^{36\times 36} \ni E^{5'} = \begin{bmatrix} & & & & & E\\ & & & & I & \\ & & & E & & \\ & & I & & & \\ & E & & & & \\ I & & & & & \end{bmatrix}, \quad \mathbb{R}^{36\times 36} \ni E^{3'} = \begin{bmatrix} & & & & & I\\ & & & & E & \\ & & & I & & \\ & & E & & & \\ & I & & & & \\ E & & & & & \end{bmatrix}$$

and $\overline{\beta}\overline{\alpha}$ is the complementory sequence to $\alpha\beta$. Show that for any sequence S:

$$\begin{aligned} K(\overline{S}, \mathcal{P}) &= E_N K(S, \mathcal{P}) E_N, \\ \mu(\overline{S}, \mathcal{P}) &= E_N \mu(S, \mathcal{P}), \end{aligned}$$

so that $\rho(\overline{\mathbf{w}}; \overline{S}, \mathcal{P}) = \rho(\mathbf{w}; S, \mathcal{P})$, where $\overline{\mathbf{w}} = E_N \mathbf{w}$.

3. Using part 2), how many of the conditions in part 1) are independent?

2 Zero entries in the cgDNA+ parameter set

i) Describe all of the restrictions on the cgDNA+ parameters $K^{\alpha\overline{\alpha}}, \sigma^{\alpha\overline{\alpha}}$ for each of the palindromic dimer steps $\alpha\overline{\alpha}$, $\alpha \in \{A, T, C, G\}$.

ii) If S is a palindromic sequence, i.e., $\overline{S} = S$, what are the corresponding restrictions on the reconstructions, $K(S), \sigma(S)$, $\mu(S)$.

3 Total number of unknowns in a cgDNA+ parameter set

Let $\mathcal{P} = \left\{K^{\alpha\beta} \in \mathbb{R}^{42\times42}, \sigma^{\alpha\beta} \in \mathbb{R}^{42}, K^{5'\alpha\beta} \in \mathbb{R}^{36\times36}, \sigma^{5'\alpha\beta} \in \mathbb{R}^{36} | \alpha\beta \in D\right\}$, where D is the set of all dimers formed using the alphabet $M = \{A, T, G, C\}$, be a cgDNA+ parameter set. Using all the symmetry conditions (i.e. Crick-Watson symmetries mentioned in exercise 1 and palindrome restrictions explained in exercise 2, find total number of independent scalars in parameter set $\mathcal{P}$.