Mathematical Modelling of DNA — Version 1
Prof. John Maddocks
Session 5: Solutions — A. Patelli

1 Effect of a point mutation on the Shape and on the Stiffness

For questions 1-4 is useful to compute the difference $dx = x_1 - x_2$, where x_i is the ground-state of sequence S_i. In Figure 1 we show the values of the helical parameters of dx.

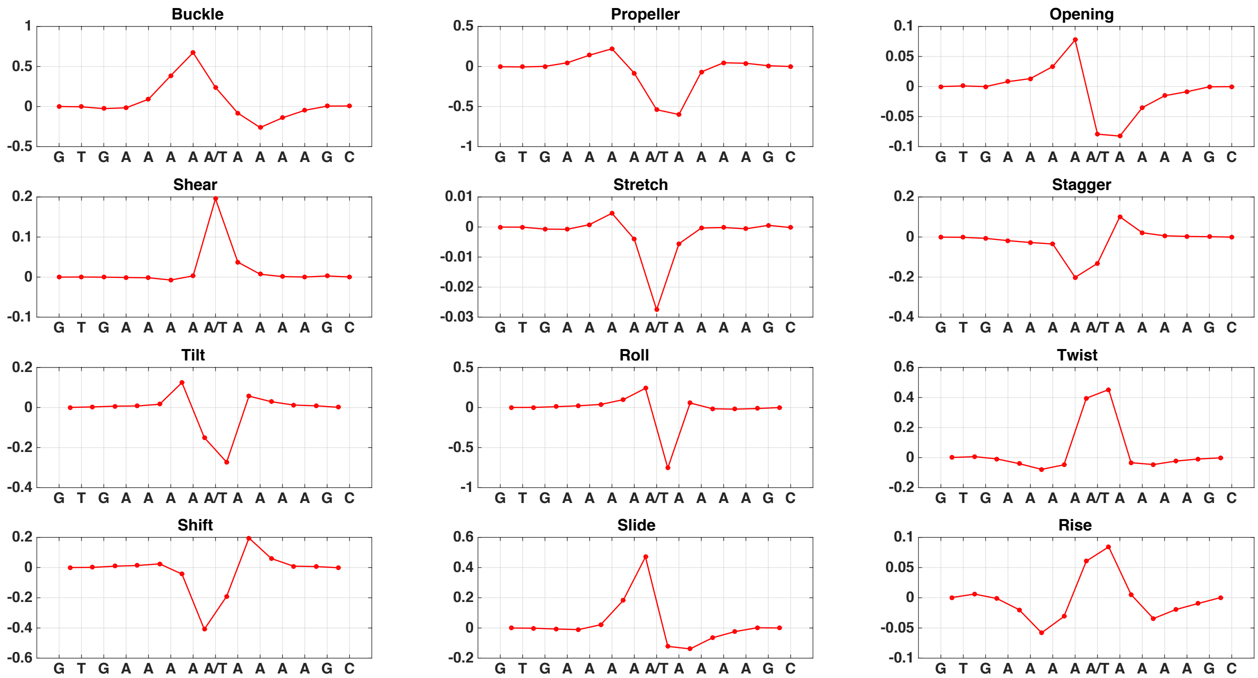

Figure 1: Values of the differences in the helical parameters between ground-state of S_1 and ground-state of S_2.

In Figure 2 we show, using the command `spy`, the difference $dK = K_1 - K_2$, where K_i is the stiffness matrix for sequence S_i. As already done in session 4 exercise 4.1.2, a point mutation leads to a local change in stiffness.

2 On the symmetry of the coordinates system

Useful matlab function for this exercise:

1. The complementary sequence of S is $\bar{S} = GCTTTTTTTTTCAC$. For checking that $\mathbf{x}(S) = E_n\mathbf{x}(\bar{S})$ one can compute $\|\mathbf{x}(S) - E_n\mathbf{x}(\bar{S})\|$. While for the stiffness one can use the command `spy` in order to visualize the difference $dK = K(S) - E_nK(\bar{S})E_n$. Be aware that the command `spy` shows all non zero entries of the matrix or vector passed as argument. In order to filter out small entries one can use the following trick: `spy( abs(dK)>1e-10 )`.

2. The sequence S is a palindrome which means that $S = \bar{S}$. This implies the following:

$$
\begin{aligned}
\mathbf{x}(S) &= E_n\mathbf{x}(\bar{S}) = E_n\mathbf{x}(S), \\
K(S) &= E_nK(\bar{S})E_n = E_nK(S)E_n.
\end{aligned}
$$

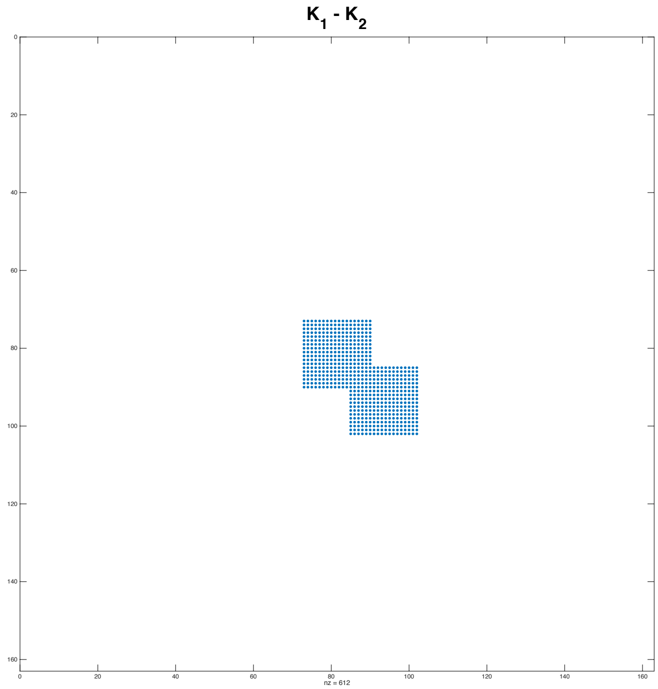

Figure 2: Difference between stiffnesses for S_1 and S_2.

From the above equation for the stiffness matrix K, and by using the first part of this question, we can conclude that $K(S) - E_n K(S) E_n$ is the zeros matrix. Finally in order to understand why the Shift in junction 6 is zero it is important to understand what happen to $\mathbf{x}(S)$ when multiplied by E_n. More precisely what happen to the intras and the inters of $\mathbf{x}(S)$ See also the solution of the exercise 4.2 of this sheet. There will be an exercise later on in the semester where we will better explore the action of the matrix E_n on the ground-state and on the stiffness of palindromic sequences.

3 Properties of SO(3) matrix representation

1. Let $P \in O(3)$ and $M \in \mathbb{R}^{3\times3}$ a diagonalizable matrix , with $R \in \mathbb{F}^{3\times3}$ such that $M = RDR^{-1}$, $D = diag(\lambda_1, \lambda_2, \lambda_3)$.
We remark that $(P^T MP)^2 = (P^T MP)(P^T MP) = P^T MPP^T MP) = P^T M^2 P$, because $P^T P = I$. Thus we have that for any power $\alpha \in \mathbb{N}$ we have

$$(P^T MP)^\alpha = (P^T MP)(P^T MP)\cdots(P^T MP) = P^T M^\alpha P.$$

Let take $\alpha \in \mathbb{R} \setminus \mathbb{N}$ and let us use the decomposition of $M = RDR^{-1}$. We obtain that $P^T MP = P^T RDR^{-1}P$. Define $\tilde{R} = P^T R$ thus, $P^T MP = \tilde{R}D\tilde{R}^{-1} = \tilde{M}$. Now, $\tilde{M} \in \mathbb{R}^{3\times3}$ and is diagonalizable. Thus, we can apply the Definition 1 of the exercise sheet to obtain the generalized power $\tilde{M}^\alpha$,i.e,

$$(P^T MP)^\alpha = \tilde{M}^\alpha = \tilde{R}D^\alpha\tilde{R}^{-1} = P^T RD^\alpha R^{-1}P = P^T M^\alpha P. \tag{1}$$

The statement is proven.

2. For what follows, $P \in O(3)$ and $Q \in SO(3)$.

- Define $\overline{u} := Cay(P^TQP)$, from the definition on the exercise sheet we obtain that

$$[\overline{u}\times] = (P^TQP + \mathbf{I})^{-1}(P^TQP - \mathbf{I}) \tag{2}$$

Since $P^TP = \mathbf{I}$ we have that $(P^TQP \pm \mathbf{I}) = P^T(Q \pm \mathbf{I})P$. Moreover by using the result of exercise (3.1) we have that $(P^T(Q \pm \mathbf{I})P)^{-1} = P^T(Q \pm \mathbf{I})^{-1}P$, thus we obtain that

$$[\overline{u}\times] = P^T(Q + \mathbf{I})^{-1}(Q - \mathbf{I})P = P^T[u\times]P = [|P|P^Tu\times], \tag{3}$$

which implies

$$Cay(P^TQP) = \overline{u} = |P|P^Tu = |P|P^TCay(Q). \tag{4}$$

- Again define $\overline{u} := Cay(Q^T)$, as before we remark that $(Q^T \pm \mathbf{I}) = (Q \pm \mathbf{I})^T$. Thus, we obtain

$$[\overline{u}\times] = (Q + \mathbf{I})^{-T}(Q - \mathbf{I})^T = [(Q + \mathbf{I})^{-1}(Q - \mathbf{I})]^T = [u\times]^T = -[u\times]. \tag{5}$$

We used the fact that $(Q + \mathbf{I})^{-1}$ and $(Q - \mathbf{I})$ commute. Finally we obtain that

$$Cay(Q^T) = \overline{u} = -u = -Cay(Q). \tag{6}$$

4 Proof of the change of reading strand transformation

1. Let $(R, r)^-$ and $(R, r)^+$ be two frames and recall the following notion:

- the Cayley vector of the relative rotation from "minus" to "plus" : $u = Cay(R^-R^+) \in \mathbb{R}^3$
- the mid frame (R, r): $R = R^-([R^-]^TR^+)^{\frac{1}{2}}$, $r = \dfrac{1}{2}(r^- + r^+)$
- the relative translation: $v = R^T(r^+ - r^-) \in \mathbb{R}^3$,

Define now the analogous of u and v but in the frames $(\overline{R}, \overline{r})^pm$ by $\overline{u}$ and $\overline{v}$,and let $P \in O(3)$. We want now to find the transformation between the rotations $\overline{u}$ and u:

$$\begin{aligned}
\overline{u} &= Cay(\overline{R}^-\overline{R}^+) = Cay(P^T[R^+]^TR^-P) && (7)\\
&= |P|P^TCay([R^+]^TR^-) = |P|P^TCay(\big[[R^-]^TR^+\big]^T) && (8)\\
&= |P|P^TCay([R^-]^TR^+) = |P|P^Tu && (9)
\end{aligned}$$

Before computing the transformation between the translational part $\overline{v}$ and v we observe that the mid frames (R, r) can also be defined as the mid rotation from "plus" to "minus". In fact

$$\begin{aligned}
[R^-([R^-]^TR^+)^{\frac{1}{2}}]^TR^+([R^+]^TR^-)^{\frac{1}{2}} &= ([R^-]^TR^+)^{\frac{T}{2}}[R^-]^TR^+([R^+]^TR^-)^{\frac{1}{2}}\\
&= ([R^-]^TR^+)^{\frac{T}{2}}([R^-]^TR^+)^{\frac{1}{2}}([R^-]^TR^+)^{\frac{1}{2}}([R^+]^TR^-)^{\frac{1}{2}}\\
&= ([R^-]^TR^+)^{\frac{1}{2}}([R^+]^TR^-)^{\frac{1}{2}}\\
&= ([R^-]^TR^+)^{\frac{1}{2}}([R^-]^TR^+)^{\frac{T}{2}}\\
&= I,
\end{aligned}$$

thus $R = R^-([R^-]^TR^+)^{\frac{1}{2}} = R^+([R^+]^TR^-)^{\frac{1}{2}}$. Now we can compute the mid frame $(\overline{R}, \overline{r})$:

$$\begin{aligned}
\overline{R} &= \overline{R}^-([\overline{R}^-]^T\overline{R}^+)^{\frac{1}{2}} = R^+P(P^T[R^+]^TR^-P)^{\frac{1}{2}}\\
&= R^+([R^+]^TR^-)^{\frac{1}{2}}P = RP
\end{aligned}$$

Thus we can find the transformation from $\overline{v}$ and v:

$$\overline{v} = \overline{R}^T(\overline{r}^+ - \overline{r}^-) = P^TR^T(r^- - r^+) = -P^TR^T(r^+ - r^-) = -P^Tv \tag{10}$$

2. The DNA fragment (with sequence $S = X_1, X_2, \ldots, X_N$) we are considering is described by the internal coordinates

$$x = ((\eta_1, w_1), (u_1, v_1), \ldots, (u_{N-1}, v_{N-1}), (\eta_N, w_N)) = (y_1, z_1, \ldots, z_{N-1}, y_N),$$

where $y_i = (\eta_i, w_i) \in \mathbb{R}^6$ are the intra base–pair variable and $z_l = (u_l, v_l) \in \mathbb{R}^6$ are the inter base–pair variables.

We first write down the base–pair frames and junction frames associated to $\{(R_i, r_i)^C, (R_i, r_i)^W\}_{i=1}^N$:

Define the i–th base–pair frame

For all $i = 1, 2, \ldots, N$:

- $R_i = R_i^C([R_i^C]^T R_i^W)^{\frac{1}{2}}$
- $r_i = \dfrac{1}{2}(r_i^C + r_i^W)$

Define the l–th junction frame

For all $l = 1, 2, \ldots, N-1$:

- $J_l = R_l(R_l^T R_{l+1})^{\frac{1}{2}}$
- $j_l = \dfrac{1}{2}(r_l + r_{l+1})$

For the change of reading strand transformation the matrix $P \in O(3)$ we have to chose is

$$P = \begin{bmatrix} 1 & 0 & 0 \\ 0 & -1 & 0 \\ 0 & 0 & -1 \end{bmatrix}.$$

The next step is to identify the frames of the starting configuration with the frames of the transformed one. It is easy to see that the relation between the two configuration is:

$$\begin{aligned} \overline{R}^C_{N+1-i} = R_i^W P \quad &, \quad \overline{r}^C_{N+1-i} = r_i^W \\ \overline{R}^W_{N+1-i} = R_i^C P \quad &, \quad \overline{r}^W_{N+1-i} = r_i^C \\ \overline{R}_{N+1-i} = R_i P \quad &, \quad \overline{r}_{N+1-i} = r_i \\ \overline{J}_{N-l} = J_l P \quad &, \quad \overline{j}_{N-l} = j_l. \end{aligned} \tag{11}$$

Define now the two linear transformation of the indices: $\sigma(i) = N + 1 - i$ and $\gamma(l) = N - l$. By using Exercise 4.1 we can define the internal coordinate of the transformed configuration:

Inter variables

$$\forall l = 1, \ldots, N-1 \begin{cases} \overline{u}_{\gamma(l)} = -P^T u_l \\ \overline{v}_{\gamma(l)} = -P^T v_l \end{cases} \Rightarrow \overline{z}_{\gamma(l)} = diag(-P^T, -P^T) z_l = E z_l.$$

Here for each l we used the Exercise 4.1 with $\{(R_l, r_l), (J_l, j_l), (R_{l+1}, r_{l+1})\}$ and the transformation P.

Intra variables

$$\forall i = 1, \ldots, N \begin{cases} \overline{\eta}_{\sigma(i)} = -P^T \eta_i \\ \overline{w}_{\sigma(i)} = -P^T w_i \end{cases} \Rightarrow \overline{y}_{\sigma(i)} = diag(-P^T, -P^T) y_i = E y_i.$$

Here for each i we used the Exercise 4.1 with $\{(R_i^C, r_i^C), (R_i, r_i), (R_i^W, r_i^W)\}$ and the transformation P.

Finally the change of reading strand transformation implies a change also on the sequence of the transformed DNA, i.e, $\overline{S} = \overline{X}_N, \overline{X}_{N-1}, \ldots, \overline{X}_1$. Now, the internal coordinates of the DNA fragment with sequence $\overline{S}$ is described by

$$\overline{x} = (\overline{y}_1, \overline{z}_1, \ldots, \overline{z}_{N-1}, \overline{y}_N) \tag{12}$$

Using the indices transformation σ and γ, and the relation on the inter and intra variables, we can rewrite $\overline{x}$ as

$$\overline{x} = (E y_N, E z_{N-1}, E y_{N-1}, E z_{N-2}, \ldots, E z_1, E y_1) = \begin{bmatrix} & & & E \\ & & E & \\ & \iddots & & \\ E & & & \end{bmatrix} \begin{bmatrix} y_1 \\ \vdots \\ z_{N-1} \\ y_N \end{bmatrix} \tag{13}$$