Mathematical Modelling of DNA
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1 Effect of a point mutation on the Shape and the Stiffness

For this exercise use the cgDNAweb with the **parameter set 2 (PS2)**.
In this exercise we will show how a single point mutation in a given sequence (change of a letter) will lead to a change on the reconstruction of the shape coordinates. For that consider the two following sequences:

S_1 = GTGAAAAAAAAAGC,

S_2 = GTGAAAATAAAAGC.

Using cgDNAweb construct the shapes and the stiffness matrices for S_1 and S_2. Then do the following:

1) Compare the 3D structure of the ground-states. What can you say?
2) For which base pair the change of Stagger is biggest when passing from S_1 to S_2?
3) For which base pair the change of Propeller is biggest when passing from S_1 to S_2?
4) Of all the junctions, where the value of Roll changes by more than 1% when passing from S_1 to S_2, which junction is closest to the end of the oligomer?
5) What do you expect to be the changes in the stiffness matrices?

2 On the symmetry of the coordinate system

Let $\mathcal{P}$ be a cgDNA parameter set. For a base $X \in \{A,T,G,C\}$ we note its complementary base by $\overline{X}$. Moreover if $S = X_1X_2\dots X_{n-1}X_n$ is a sequence, we note by $\overline{S} = \overline{X}_n\overline{X}_{n-1}\dots\overline{X}_2\overline{X}_1$ its complementary. For a sequence $S = X_1\dots X_n$ we define

$$E_n = \begin{bmatrix} & & & E \\ & & E & \\ & \iddots & & \\ E & & & \end{bmatrix},$$

where $E = diag(-1,1,1,-1,1,1)$. In fact, the matrix E_n is a block trailing–diagonal matrix with $2n-1$ copies of E.

1) Consider again S_1 from exercise 1 and let $S = S_1$. Write down the sequence $\overline{S}$. Using the cgDNA package construct the shapes ($\mathbf{x}(S)$ and $\mathbf{x}(\overline{S})$) and the stiffness matrices ($K(S)$ and $K(\overline{S})$) and check that:

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

2) Take a sequence S = CGCGAATTCGCG (Drew-Dickerson dodecamer) and construct the shape vector $\mathbf{x}(S)$ and the stiffness matrix $K(S)$, then compute $E_n\mathbf{x}(S)$ and $E_nK(S)E_n$. What is the number of entries in K, where the change between K and $E_nK(S)E_n$ is bigger than 1%? What is the value of Shift in junction 6 of $\mathbf{x}$(S) and why?

3 Properties of SO(3) matrix representation and square roots

3.1 On the general power of diagonalizable matrices

First we define the general power of a diagonalizable matrix (which include the case of interest to us, $M \in SO(3)$):

Definition 1. *Let $M \in \mathbb{R}^{3\times3}$, be a diagonalisable matrix, so that there exists a matrix $R \in \mathbb{R}^{3\times3}$, or in $\mathbb{C}^{3\times3}$, such that $M = RDR^{-1}$, with $D = diag(\lambda_1, \lambda_2, \lambda_3)$. The generalised power of M is denoted by M^α, $\alpha \in \mathbb{R}$, and is defined as*

$$M^\alpha = RD^\alpha R^{-1} \tag{1}$$

where

$$D^\alpha = diag(\lambda_1^\alpha, \lambda_2^\alpha, \lambda_3^\alpha). \tag{2}$$

Note that if

- $\alpha = -1$, M^α is the inverse of M,
- $\alpha = \frac{1}{2}$, M^α is the principal square root of M.

By applying Definition (1) to a matrix $Q \in SO(3)$ we have that

$$Q^{\frac{1}{2}} = Hdiag\left(\exp\left(i\frac{\theta}{2}\right), \exp\left(-i\frac{\theta}{2}\right), 1\right)H^*, \ H \text{ is hermitian, and } HH^* = \mathrm{I},$$

where θ is the rotation angle of Q. Let now $P \in O(3)$ and $M \in \mathbb{R}^{3\times3}$ a diagonalizable matrix, prove that

$$(P^T MP)^\alpha = P^T M^\alpha P, \ \forall \alpha \in \mathbb{R}. \tag{3}$$

[Note: for the case $\alpha \in \mathbb{N}$ there is no need to use the Definition (1)]

3.2 More properties of the Cayley transform

We want now to prove two properties of the Cayley transform of $Q \in SO(3)$, defined as

$$u = Cay(Q) \Leftrightarrow [u\times] = (Q + \mathbf{I})^{-1}(Q - \mathbf{I}),$$

where $u \in \mathbb{R}^3$ and $Q \in SO(3)$. Prove that:

1. $Cay(P^T QP) = |P|P^T Cay(Q)$, $\forall P \in O(3)$.

2. $Cay(Q^T) = -Cay(Q)$.

4 Proof of the change of reading strand transformation

In the lecture we have discussed the *change of reading strand* transformation. In the first part of this exercise we will prove a general result for two rigid bodies on the change of framing when the transformation is a constant rotation, while in the second part we will focus on the application of the latter case on the DNA and more precisely we will derive the change of variable needed for the change of reading strand transformation.

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

i) the Cayley vector of the relative rotation from "minus" to "plus" : $u = Cay([R^-]^T R^+) \in \mathbb{R}^3$

ii) the mid frame (R, r): $R = R^-([R^-]^T R^+)^{\frac{1}{2}}$, $r = \frac{1}{2}(r^- + r^+)$

iii) the relative translation: $v = R^T(r^+ - r^-) \in \mathbb{R}^3$

Let now $P \in O(3)$ and define

$$\overline{R}^{\pm} = R^{\mp} P.$$

Find the transform

$$u \mapsto \overline{u} \tag{4}$$

$$v \mapsto \overline{v}, \tag{5}$$

where $\overline{u}, \overline{v} \in \mathbb{R}^3$ are the internal coordinate of the rigid bodies $(\overline{R}, \overline{r})^{\pm}$.

2. Consider now a fragment of DNA of length N. Using the convention of the change of reading strand transformation and the part a) of this exercise, write explicitly the change of variable of the internal coordinates $x = ((\eta_1, w_1), (u_1, v_1), (\eta_2, w_2), (u_2, v_2), \ldots, (u_{N-1}, v_{N-1}), (\eta_N, w_N))$ by considering the transformation between

$$\left\{(R_i, r_i)^C, (R_i, r_i)^W\right\}_{i=1}^N \mapsto \left\{(\overline{R}_k, \overline{r}_k)^C, (\overline{R}_k, \overline{r}_k)^W\right\}_{k=1}^N.$$

$\overline{R}^C$, and $\overline{R}^W$ are defined in the same way as are defined in 2.1).
[Note: here we choose W = "plus" and C = "minus".]

5 Downloading and compiling the cgDNAmc code

Download and compile on your machine the cgDNAmc code `http://lcvmwww.epfl.ch/research/cgDNA/downloads.php`. Follow the on–line documentation and report anything unclear. Next week we will make Monte Carlo computations with the cgDNA model.