Computational Biology: Final Examination 23. Februar 2015

Brock
Mabrouk / Putz / Schneider / Werner

Name: .....

First name: .....

Matr.-Nr.: .....

Time: 75 Minuten

- Please write legibly and do **not** use a red pen.
- Write your name and your student ID (Matrikelnummer) on *all* pages *now*.

	Points	Score
1	25	
2	15	
3	14	
4	20	
5	12	
6	14	
Σ	100	

1 (25 points): Molecular Biology and Protein Structure

1.1. (5 points) What is the central dogma of molecular biology?

1.2. (6 points) Consider the following bonds of a protein backbone.

- C_α-C
- C-N
- N-C_α

Exactly two of these bonds are rotatable and account mostly for the conformational diversity of the protein backbone. Please mark exactly these two bonds and name the corresponding angles. *Important note: This question will only be graded if exactly two bonds are marked.*

1.3. (6 points) Name three molecular forces that are responsible for stabilizing proteins.

1.4. (3 points) Name three secondary structures that are most common in protein structures.

1.5. (5 points) A mutation that changes an alanine residue in the core of a protein to valine is found to lead to loss of activity. However, activity is regained when a second mutation at a different position in the core changes an isoleucine to glycine.

How might this second mutation lead to a restoration of activity?

2 (15 points): Monte Carlo

Conformational sampling of protein structures is often done by Monte Carlo (MC) algorithms. In an MC simulation, an initial conformation is randomly generated and new conformations are sampled by random moves. The new conformation is accepted or rejected based on an scoring function.

2.1. **(4 points)** What would happen if you start search at the given initial conformation and only accept conformations that are lower in energy than the current conformation? Draw one possible outcome into the plot.

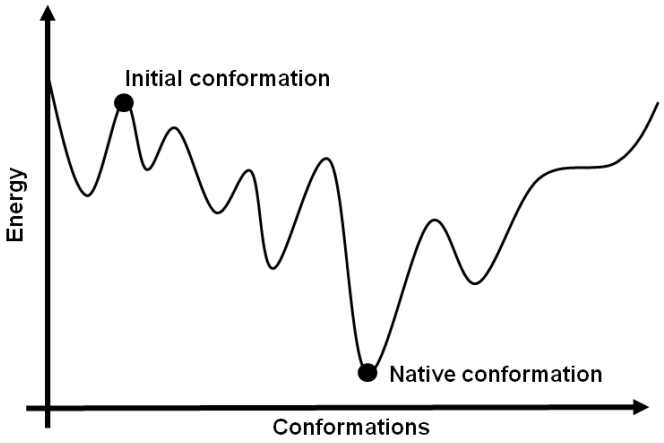

Figure 1: Cartoon of an energy landscape.

2.2. (6 points) Metropolis-Monte Carlo algorithm

1. What factors determine whether a new conformation is accepted or refused in a Metropolis-Monte Carlo algorithm? Write down both factors.

2. What is the difference of the Metropolis-Monte Carlo algorithm to a Monte Carlo algorithm that only accepts conformations that are lower in energy?

3. Which parameter can be tuned to change the explorative behaviour of the Metropolis-Monte Carlo algorithm?

2.3. **(5 points)** Imagine that you have initialized a Metropolis-Monte Carlo algorithm with a high temperature and your algorithm has found the global minimum after a number of steps.

1. Please choose one of the following:
   (1) The algorithm will stay in the global minimum or
   (2) The algorithm will leave the global minimum.
   Please explain your decision.

2. How does simulated annealing improve the behaviour of the Metropolis-Monte Carlo algorithm?

3 (14 points): Dynamic Programming

3.1. (6 points) Write down the recursive formula for the Smith-Waterman local alignment algorithm.

3.2. (8 points) Compute the local alignment matrix for two DNA sequences TCCGA and TACGCA. Please give the resulting optimal alignment and its score.
The score for deletions and insertions is -7 . The score for mismatches is -5. The score for a match is 10.

4 (20 points): Bioinformatics and Comparative Modeling

4.1. **(6 points)** A biologist friend needs to determine a structure of a protein for a project she is working on. You volunteer to help. You run both comparative modeling and ab initio structure prediction and generate a number of decoys from each method.

1. How do you choose the method (comparative modeling or ab initio) from which you will select your prediction (decoy)? (Please give one property or feature that you will use to make the choice and explain your reasoning)
2. How do you select the prediction (decoy) that you will return to her? (Please give one property or feature that you will use to select the decoy and explain your reasoning)

4.2. **(6 points)** List and describe the four main components/steps of a classical comparative modeling algorithm.

4.3. **(8 points)** Pairwise sequence alignment is a simple technique used in comparative modeling.

1. What is the biological motivation behind the use of pairwise sequence alignment in comparative modeling?
2. Explain the difference between local alignment and global alignment. Include one example for clarification.
3. What is the motivation behind substitution matrices?
4. How are substitution matrices used in a sequence alignment algorithm?

5 (12 points): Jacobian

Figure 4 depicts the previously introduced 3-DoF kinematic chain consisting of two revolute joints q_1 and q_2 followed by one prismatic joint q_3. The link lengths are given by L_1, L_2 and L_3.

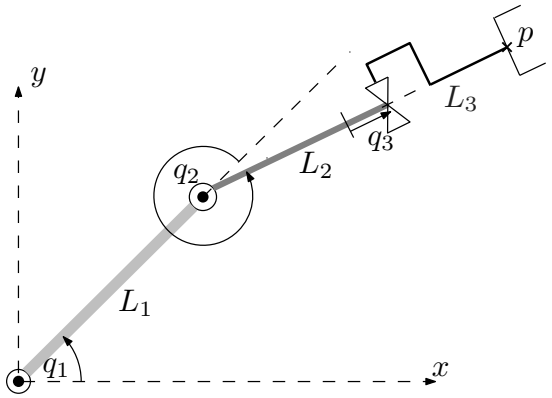

Figure 2: 3-DoF kinematic chain (RRP)

We want to control $\mathbf{p}$ using the Jacobian. Let $\mathbf{J}$ denote the end-effector Jacobian of the robot in Figure 4.

5.1. **(4 points)** Give an intuition for the meaning of $\mathbf{J}_{2,2}$, i.e. the entry in the second column of the second row of the Jacobian!

5.2. **(4 points)** What is the rank of $\mathbf{J}$?

(The rank of a matrix can be defined as the number of its linearly independent rows or columns.)

5.3. **(4 points)** Draw a configuration of the robot in Figure 4 where the rank of the Jacobian is 2!

Figure 3: Draw your solution in here.

6 (14 points): Forward Kinematics

6.1. **(14 points)** Consider the depicted 3-DoF kinematic chain consisting of two revolute joints q_1 and q_2 followed by one prismatic joint q_3. The link lengths are given by L_1, L_2 and L_3.

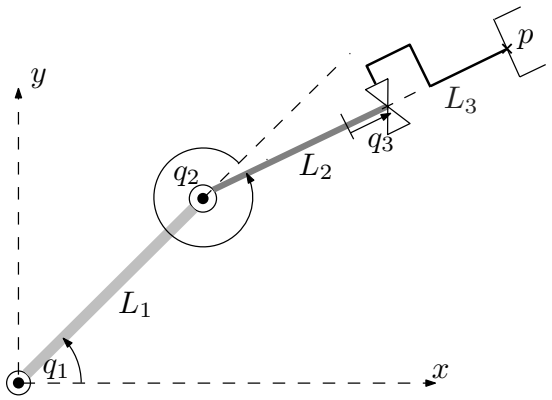

Figure 4: 3-DoF kinematic chain

Describe the position and orientation of the end-effector $p = [x, y, \theta]^T$ as a function of the joint variables q_1, q_2 and q_3 (forward kinematics).