GENOMIC PROJECT

Genom-1 Group

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1 Introduction

We were given the objective to build a program with actual applications in current genomic problems. Several resource files can be given by the user, such as a genomic sequence, a Position Weight Matrix (PWM) or Position-Specific Scoring Matrix (PSSM), affinity scores along a specific sequence... The idea is to offer different outputs that can help the user to solve his/her problem. The output can be a list of binding sites present on a chromosome, an affinity score for a given binding site, a PWM (or a PSSM), or a graphic representation of the consensus sequence determined by the PMW.

2 A bit of biology

Transcription Factors refer to any proteins that are required to initiate or regulate transcription in eucaryotes. They include gene regulatory proteins, general transcription factors, co-activators, co-repressors, histone-modifying enzymes, and chromatin remodeling complexes. Transcription is the process by which a gene?s DNA sequence is converted into a complementary messenger RNA molecule, itself undergoing translation, process involved in the production of proteins. The study of transcription factors and regulatory proteins is of critical importance in the understanding of, for example, genetic diseases.

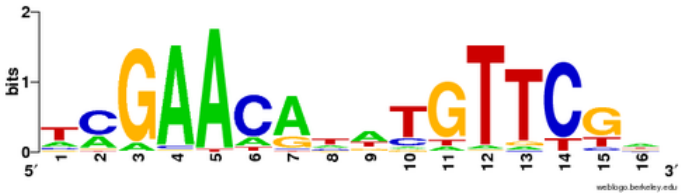
Such proteins comprise one or several **binding domains** in their active conformation, which permit them to bind to the DNA sequence. The amino acids of the binding domains bind specifically to DNA nucleic acids by complementarity. These binding sites, referred as motifs, are described with a **Position Weight Matrix** (Fig.**??**) (also known as **Position-Specific Scoring Matrix**), which contains the probability that each nucleic acid (A ,C, G or T) is at each position of the motif. Therefore, the probability of a specific motif may be known and comparison of the probabilities - referred as scores - to a threshold value may *distinguish relevant binding sites from non-functional sites* of similar sequences. Binding sites for known proteins may thus be found in different regions of the genome. The PWN also permits the determination of the **consensus sequence** representation (Fig.**??**), which gives an idea on the several motifs that may be relevant. This latter representation constitutes a visual representation of the motif : the sizes of the letter is proportional to their probability.

Figure 1: Example of a PWM matrix .

$$\begin{pmatrix} 0.9913 & 0.0019 & 0.0044 & 0.0024 \\ 0.0045 & 0.0031 & 0.9611 & 0.0313 \\ 0.0032 & 0.9915 & 0.0019 & 0.0034 \\ 0.8917 & 0.0019 & 0.0089 & 0.0975 \\ 0.6241 & 0.2510 & 0.0059 & 0.1187 \\ 0.7289 & 0.1045 & 0.0116 & 0.1550 \\ 0.3048 & 0.4911 & 0.0045 & 0.1996 \end{pmatrix} \begin{matrix} 1 \\ 2 \\ \\ \\ ... \\ \\ \\ L=7 \end{matrix}$$

A C G T

Figure 2: Logo of a consensus sequence.



3 Download the program

To download the program, go to : https://github.com/EPFL-SV-cpp-projects/genom-1. Open a terminal and go to the directory where you want the program, then type "git clone **https://github.com/EPFL-SV-cpp-projects/genom-1".** The genom-1 folder and all of its content will be copied into your directory, you can then compile and execute the program.

4 Compilation and execution

To compile and execute the program, a fews steps are required. Make sure you are in the genom-1 folder and then :

rm –rf build and **mkdir build** to make sure an empty build folder is crated

cmake../

make

And then you have several options

If you want to see the documentation with the doxyfile, describing more precisely the different classes and fonctions involved in the program you will then have to write **make doc**

If you want to execute the program, then do **../src/Main**

If you want to run the tests of the program, then do **make test**

5 The functionalities of the program

When you execute the program, a menu will appear, proposing you a list of outputs designed by their numbers. You can choose the task the program must do by hitting '1', '2' or '3' or '4'. Then you will be asked to provide the inputs (if the program needs a file you can write its name like "$example.fasta$"). Here are the mains functionalities of the program :

1.- Being able to read a DNA sequence and a PWM (or/and it's logarithmic version) and give as output the list of site along the genome where the protein is gonna attach.

2.- Being able to read a DNA sequence, a list of sites and their respective binding score (the product of the probabilities of each nucleotide along the sequence) and output a PWM (or/and it's logarithmic version).

3.- Based on the matrix or based on the binding scores and list of sites, being able produce a sequence logo.

4.- Using a matrix and a sequence, give the list of all possibles sites that are above a threshold given by the user.