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Sequence analysis

OligoFaktory: a visual tool for interactive oligonucleotide design

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ABSTRACT

Summary: The OligoFaktory is a set of tools for the design, on an arbitrary number of target sequences, of high-quality long oligonucleotide for micro-array, of primer pair for PCR, of siRNA and more. The user-centered interface exists in two flavours: a web portal and a standalone software for Mac OS X Tiger. A unified presentation of results provides overviews with distribution charts and relative location bar graphs, as well as detailed features for each oligonucleotide. Input and output files conform to a common XML interchange file format to allow both automatic generation of input data, archiving, and post-processing of results. The design pipeline can use BLAST servers to evaluate specificity of selected oligonucleotides.

Availability: The web portal http://ueg.ulb.ac.be/oligofaktory/; the software for Macintosh: http://www.oligofaktory.org/

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The OligoFaktory groups dedicated several bioinformatic tools, embedded in a common framework. The dynamic and interactive application provides consistent form-based input interface and presentation of outputs. Each application is dedicated to a specific objective and provides great control over specific parameters and constraints. The project is aimed at assisting researchers for a painless, rapid, automated and reliable design.

Each oligonucleotide design application has been implemented using a common multilevel optimization pipeline (Schretter and Milinkovitch, 2005) shown in Figure 3. The optimization integrates a numerical approach to the minimization of undesirable interactions such as hairpins, homodimers and heterodimers. Furthermore, we maintain diversity in the population of candidate solutions to ensure domain exploration. Specificity evaluation against any official NCBI database or any custom-made database is provided by using a BLAST server.

The OligoFaktory performs the complete design process, from raw query sequences data submission to ordering of designed oligonucleotides. Hence, the application federates a collection of independent, but complementary tools that can be combined into a very large number of possible scenarii. As shown in Figure 2, users will produce easily a set of results by using a succession of complementary actions.

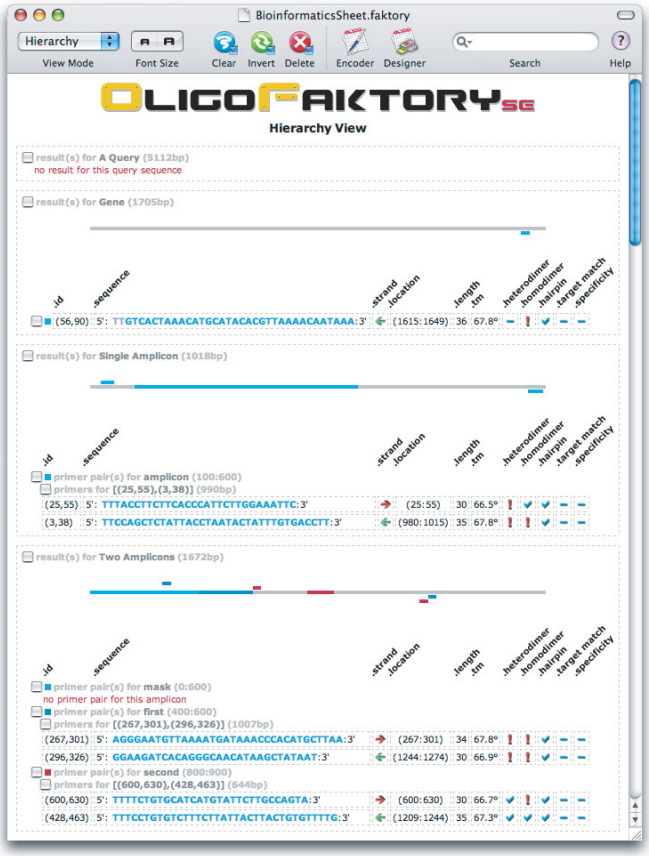

Fig. 1. The main screen of the OligoFaktory Standalone Edition. The toolbar allows one-click access to any functionality and provides controls to choose the presentation of results. Colored bargraphs show the position of amplicons and oligonucleotides, relative to their query sequence.

A form is associated with each tool to fetch parameters from users' input. Input forms ensure validation of parameters and consistency of presentation. The OligoFaktory also reads FASTA

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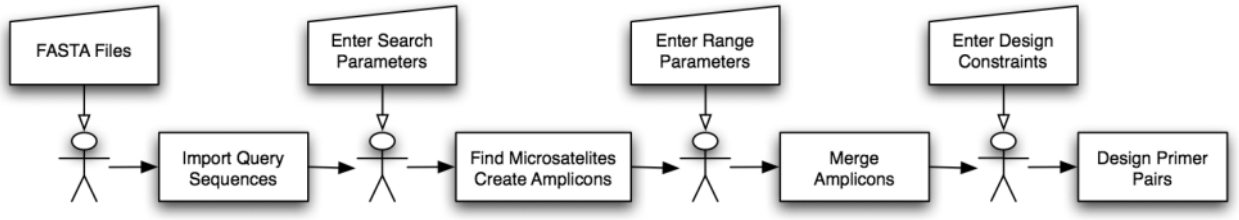

Fig. 2. An example scenario of interactive primer design. Stickmans indicate user-interactivity steps, namely, the edition of input forms. Rectangles indicate the processing of the current set of results by a software module.

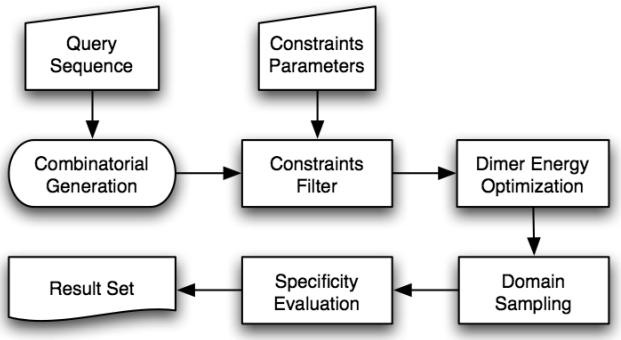

Fig. 3. The oligonucleotide selection pipeline. Each possible candidate subsequence is evaluated. After each stage, only a subset of the candidate solutions is retained.

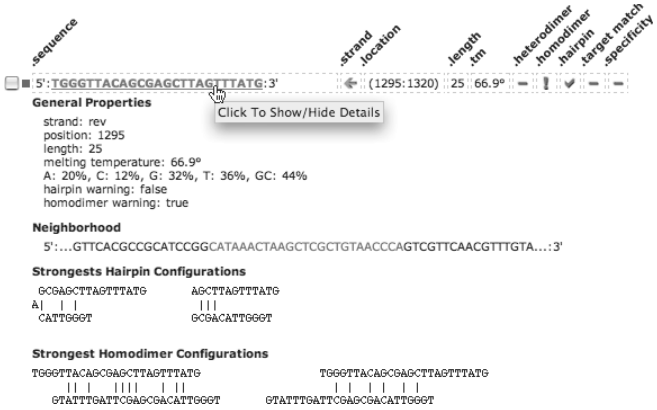

Fig. 4. The detailed view of an oligonucleotide's features. The view shows the highest energy secondary structure configurations. When specificity evaluation is used, the list of best BLAST hits is shown as well.

files and lets you export results to FASTA or a comma delimited file (CSV), readable by most spreadsheet programs.

As shown in Figure 1, a unified presentation of the output includes the list of oligo sequences together with their corresponding locations on the query sequences, their strands, their lengths and their melting temperatures. Easy-to-spot warning flags are shown in case of problems with secondary structures and/or with specificity. Moreover, detailed information on heterodimer, homodimer, hairpin, target match and specificity are obtained by clicking on the oligonucleotide sequence, as shown in Figure 4.

Several design iterations can be applied, using various actions that update the current set of results:

- The Design Long Oligo action allows designing long oligonucleotides for the development of micro-arrays.
- The Design Primer Pairs action allows designing specific primer pairs for PCR experiments.
- The Design siRNAs action allows designing optimal 19 bp siRNA with the method described in (Reynolds *et al*., 2004).
- The Find Microsatelites action identifies all microsatelites under user-specified constraints.
- The Merge Amplicons action merges amplicons which are too close to allow designing specific primer pairs.

For instance, the Merge Amplicons action will optimally be used to post-process the results of microsatelites discovered by the Find Microsatelites action. Hence, overlapping and close amplicons will be collapsed.

With the OligoFaktory standalone edition, you will be able to visualize your set of results in three different ways:

- The Hierarchy view is a complete listing that shows relative location bargraphs of queries and results.
- The Flat List view is a short listing that emphasizes leaf results, while hiding locations information.
- The Statistics view summarizes the results with charts showing the distributions of main features.

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