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Evolutionary computations and modular organization of the gene regulatory regions

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Motivation and Aim: Modular organization and functioning of gene sequences, RNA and polypeptides attracts much attention during recent decades (e.g., reviewed in [1]). Modularity in gene regulatory regions (promoters and enhancers) is crucial for our understanding of the gene functioning and evolution (e.g. [2]). In the vast area of Evolutionary Computations, inspired by the ideas and concepts from evolutionary biology, it was paid a special attention to the theoretical foundations for the evolutionary search efficacy. At first place these were Schema theorem and Building block hypothesis (by J. Holland [3]), that laid the foundation for this area in genetic algorithms (GA). On the way to further develop the theory, the Royal Road problem and Royal Road functions (RRFs) were introduced [4] and comprehensively studied [5]. Here we are considering several case-studies of the modular gene regulatory regions which could be treated as RRFs implementations in directed molecular evolution (SELEX, etc.).
Methods and Algorithms: Analytical tools from statistical mechanics, dynamical systems theory, and mathematical population genetics gave possibilities to develop a detailed and quantitative description of the search dynamics for the RRF class of problems [van Nimwegen with co-authors]. The approach bridges evolutionary computations from benchmark cases, such as RRF, which are well-understood theoretically, to biological cases, which can serve as a basis for more efficient directed molecular evolution in the test tube.
Results: By introducing GA crossover operators that perform well on RRFs, we are developing computational techniques to deal with the real design problems for bacterial and yeast promoters. In particular, we are introducing GA crossover operators that work like retroviral or sexual PCR recombination. The case examples are the bacterial promoters in comparison with the yeast promoters. We found that our algorithms are capable to achieve the polynomial efficacy of the evolutionary search. The common, standard GA algorithms are the the exponential-time algorithms for the problems.
Conclusion: Computational theory from GA can contribute to both understanding how real gene structures have evolved and to speeding up laboratory work on directed evolution of promoters and other gene regulatory elements.
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