Poster H-31

Microarray Layout and the Quadratic Assignment Problem

Authors:
Sergio A. de Carvalho Jr (*Graduiertenkolleg Bioinformatik and International NRW Graduate School in Bioinformatics and Genome R*)
Sven Rahmann (*Algorithms and Statistics for Systems Biology group, Genome Informatics, Technische Fakultät, Bielef*)

Short Abstract: We propose a new model for evaluating the quality of oligonucleotide microarrays based on the arrangement of its probes. We show that the microarray design is an instance of the quadratic assignment problem (QAP) and present the results of using a QAP heuristic to design small artificial chips.

Long Abstract:

The production of commercial oligonucleotide microarrays such as the Affymetrix GeneChip arrays is based on a parallel chemical synthesis driven by a set of photolithographic masks or micromirror arrays. Because of diffraction of light or internal reflection, untargeted spots can sometimes be accidentally activated, generating incorrect probes that can compromise the results of an experiment. The arrangement of the probes on the chip can reduce the risk of unintended illumination and play an important role in the quality of the final product.

This issue was formally addressed by Hannenhalli et al., who formulated the Border Length Minimization Problem [1]. Their formulation, however, does not take into account two practical considerations: stray light might activate not only adjacent neighbors but also probes that lie as far as three cells away from the targeted spot; and imperfections produced in the middle of a probe are more harmful than in its extremities [2].

We propose a new model called conflict index for evaluating the quality of a microarray chip [3]. The conflict index estimates the risk of synthesizing a faulty probe at a given spot. We also show that the microarray design can be modelled as an instance of the quadratic assignment problem (QAP), a classical combinatorial optimization problem. This opens up the way for using QAP heuristics for designig oligonucleotide microarrays.

The QAP has been used to model a variety of real-life problems. One of its major applications is to model the facility location problem where n facilities must be assigned to n locations. The problem is formally stated as finding a permutation of the n integers that gives an assignment of facilities to locations minimizing a cost function. We use the facility location example to model the microarray design as the problem of assigning spots to probes minimizing the sum of conflict indices. We also present a formulation for the Border Length Minimization as a special case.

The QAP is known to be NP-hard and NP-hard to approximate. Fortunately, several heuristics are available. Because of the large number of probes on real microarrays, it is not feasible to use QAP algorithms to design the layout of an entire chip. However, it is certainly

possible to use them on small sub-regions of a chip or combined with partitioning algorithms to solve smaller problem instances that can be combined to produce a final solution.

We have used an existing heuristic QAP heuristic called GRASP to design the layout of small artificial chips with promising results. At the moment we are working on several partitioning algorithms that will enable the use of QAP heuristics to design the latest million-probe microarrays.

[1] Hannenhalli S, Hubell E, Lipshutz R, Pevzner P (2002) Combinatorial algorithms for design of DNA arrays. Adv. in Biochemical Eng. / Biotechnology, 77:1–19.
[2] Kahng AB, Mandoiu I, Pevzner P, Reda S, Zelikovsky A (2003) Engineering a scalable placement heuristic for DNA probe arrays. In Proceedings of the 7th Annual International Conference on Computational Molecular Biology, 148–156.
[3] de Carvalho Jr SA, Rahman S (2006) Modeling Microarray Layout as a Quadratic Assignment Problem. Submitted.