

## Rejoinder on: Optimization and data mining in biomedicine

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First of all, we would like to thank the invited discussants for the time spent reading and commenting on our manuscript. We believe that the fruitful discussion will stimulate the interest of even more researchers and will trigger the generation of new ideas.

Floudas outlines another state-of-the-art technique for biclustering published recently that seems to be very promising compared to the available algorithms, and it has a very compact optimization formulation based on network flow. This is another example of how optimization formulation from totally different areas (e.g., network flows) can so effectively address biomedical problems.

Chaovalitwongse comments on all the presented topics where he adds some very useful literature regarding the application of optimization in the seizure prediction problem. We definitely agree with the characterization that analysis of microarray data is the holy grail of cancer research. Researchers have learned a lot (and will learn more) by carefully applying data mining methods in massive microarray datasets (Abello et al. 2002).

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This rejoinder refers to the comments available at: doi:[10.1007/s11750-009-0125-0](https://doi.org/10.1007/s11750-009-0125-0),  
doi:[10.1007/s11750-009-0127-y](https://doi.org/10.1007/s11750-009-0127-y), doi:[10.1007/s11750-009-0128-x](https://doi.org/10.1007/s11750-009-0128-x), doi:[10.1007/s11750-009-0129-9](https://doi.org/10.1007/s11750-009-0129-9),  
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Butenko comments that this article would be a nice reference for researchers that want to work on this field and he outlines the importance of the theoretical background of the presented algorithms.

Bagirov brings to the discussion another two topics relevant to the one of the papers, namely the gene selection problem and nonsmooth optimization approaches to clustering. Regarding the gene selection problem, we agree that it is indeed a very important problem. He also recognizes that this emerging area of research includes many topics though it is relatively new. We would like to add to the discussion that the gene selection problem together with the methodology mentioned by Bagirov can also be casted as a biclustering problem. In this case, every bicluster can reflect the association of a small number of genes with one disease. It is interesting to see all these alternative approaches for the same problem.

Chen et al. discuss in detail the review paper point by point, providing additional bibliographic references and approaches for the topics under discussion. As for the radiotherapy part of the paper, Chen et al. complement the literature with additional references and discussion on the additional proposed methods related to radiotherapy planning. We believe that this literature is useful for the audience; nevertheless, our goal was to give an overview of the field rather than to include all the proposed algorithms. In microarray analysis, discussants add the description of the false discovery rate (FDR). We agree that refining the feature selection process has great importance since the initial number of features is very large to handle. As for the epileptic seizure prediction part, it is interesting to note that, although in the literature there have been a lot of bivariate synchronization measures, not many researchers have tried to introduce some optimization formulation in order to enhance the selection process of the available channel pairs. These bivariate synchronization measures include, but are not limited to, spectrum based (correlation, coherence), entropy based (mutual information, etc.) and nonlinear (correlation dimension,  $STL_{\max}$ , approximate entropy, etc.) measures. We agree that the control of epileptic seizures is a central topic of epilepsy research. Our collaborators W.A. Chaovalitwongse, C.C. Liu, L.D. Iasemidis, S. Nair, O. Prokopyev and J.C. Sackellares have done pioneer work in the area of seizure prediction that the discussants summarize in their comments. We would like to comment regarding the Vagus Nerve Stimulation (VNS) (Busygin et al. 2007; Uthman et al. 2007) method that, although there have been a lot of encouraging clinical results, the exact mechanism of action is still unknown. We hope that the future medical knowledge in collaboration with control theory will provide medicine with online seizure prevention devices.

Again we would like to remind the readers that applications of optimization in biomedicine are not limited to these discussed by the authors and discussants of this paper.

Everyday we witness the formulation of new problems and new solution approaches. For example, lately there has been large amount of research on optimization challenges related to the genome problem which is not discussed in this paper. In addition, optimization has been proved useful in the area of protein folding, molecular confrontation and drug design (Pardalos et al. 1996). Also, some additional applications include the non-unique probe selection problem (Meneses et al. 2007; Ragle et al. 2007), application of support vector machines for cell death discrimination in Raman spectroscopy (Pyrgiotakis et al. 2009), etc.

Concluding we would like to thank again the discussants for the time spent reading and discussing our paper. We believe in the power of open scientific discussion, and we hope that this article will be useful for the audience of the journal.

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