Ian Holmes Department of Bioengineering University of California Berkeley, CA 94720

November 10, 2008

Dear Prof. Stormo:

Thank you very much for your attention to our earlier manuscript and for forwarding the extremely encouraging reviews.

Based on the insightful comments of the reviewers, we have made sweeping changes to the structure and presentation of the manuscript. We believe that it is greatly improved as a result.

We would be most grateful if you would consider the accompanying revised manuscript, along with the attached point-by-point response to the reviewers' earlier criticisms, describing the changes we have made.

All authors have read and approved of this manuscript.

Sincerely,

Robert K. Bradley Ian Holmes