Computational synchronization of microarray data with application to *Plasmodium falciparum*

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***Abstract*—We have developed a computational approach which predicts the protein kinases that may regulate the transition between the blood developmental stages of *Plasmodium falciparum*. To improve the accuracy of our prediction, synchronized gene expression levels are reconstructed from the observed microarray data generated by the ensembles of non-synchronized cells. Peaks in annotated protein kinase transcript levels are hypothesized to directly correlate with the period when the encoded protein kinases function temporally. Therefore, protein kinases, which putatively regulate a given developmental stage transition, are identified by their peak in synchronized gene expression levels. By analyzing publicly available microarray data set, a few protein kinases are considered to be strongly associated with developmental stage transition.**

I. Background

Microarrays are widely used to investigate the blood stage of *Plasmodium falciparum* infection. Starting with synchronized cells, gene expression levels are continually measured over the 48-hour intra-erythrocytic cycle (IDC). However, the cell population gradually loses synchrony during the experiment. As a result, the microarray measurements are blurred. In this paper, we propose a generalized deconvolution approach to reconstruct the intrinsic expression pattern, and apply it to *Plasmodium falciparum* (*P. falciparum*) IDC microarray data.

II. Methods

We develop a statistical model for the decay of synchrony among cells, and reconstruct the expression pattern through statistical inference. The proposed method can handle microarray measurements with noise and missing data. The original gene expression patterns become more apparent in the reconstructed profiles, making it easier to analyze and interpret the data. We hypothesize that reconstructed gene expression patterns represent better temporally resolved expression profiles that can be probabilistically modeled to match changes in expression level to IDC transitions. In particular, we identify transcriptionally regulated protein kinases putatively involved in regulating the *P. falciparum* IDC.

III. Results

By analyzing publicly available microarray data sets for *the P. falciparum* IDC [1], protein kinases are ranked in terms of their likelihood to be involved in regulating transitions between the ring, trophozoite and schizont developmental stages of the *P. falciparum* IDC. In our theoretical framework, a few protein kinases have high probability rankings, and could potentially be involved in regulating these developmental transitions.

IV. Conclusions

This study proposes a new methodology for extracting intrinsic expression patterns from microarray data. By applying this method to *P. falciparum* microarray data, several protein kinases are predicted to play a significant role in the *P. falciparum* IDC. Two of these (PF13_0211, PFB0815w) have recently been implicated in the schizont to ring transition [2, 3]. Another one of these identified (MAL7P1.144) has been found to influence erythrocyte membrane in both trophozoite and schizont [4]. Overall, these results suggest that further functional analysis of the other protein kinases we have predicted may reveal new insights into *P. falciparum* blood stage development.

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