

Gene Alignment for Cell Division Cycle Microarray Experiments without Sinusoidal Fittings

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1 Introduction

Microarray is the experimental technique by which we can quantize how much each gene is transcribed simultaneously. Comparing the amount of transcribed material under several experimental conditions enables us to investigate interaction of genes directly. In spite of the usefulness of this method, there are many technical limitations. Among them, the interpretation of the outcomes is the most difficult problem. For example, if we have one thousand of genes investigated under ten experimental conditions, we have matrix whose elements are more than ten times thousand of real numbers. Usually, it is very hard to interpret its meaning as it is.

In this poster, we have demonstrated that nonmetric multidimensional scaling (nMDS) has ability to figure out what is hidden in massive microarray experiments. Its ability is even superior to the confessional sinusoidal fittings, too.

nMDS is a sort of ordination methods which visualize the relationship between objects as configurations in metric space (typically, Euclidian space with low dimensions). In contrast to the conventional principal component analysis which can consider only linear transformation, nMDS can consider non-linear transformation since it try to conserve only the rank order of dissimilarities as that of distances in embedded space.

2 Method and Results

We have applied nMDS to several elutriation synchronization cell division cycle experiments of fission yeast[1, 3, 2] with employing sign-reversed correlation coefficients between gene expression profiles. Then we get circular arrangement of genes in two dimensional embeddings[4]. We have computed polar angle from this embeddings. Thus, we could succeed in getting one dimensional alignment for almost *all* genes. In Fig. 1 (a), we have shown the gene distribution associated with GO terms along polar angle defined by the circular arrangement of genes. It is obvious that polar angle can figure out gene functionality related to cell division cycle very well. On the other hand, cell cycle obtained by the conventional sinusoidal fittings has problems. For example, as shown in Figs. 1(b) and (c), genes associated with GO term “S phase of mitotic cell cycle” are not expressive at S phase. In addition to this, genes selected by sinusoidal fittings lack G2 related GO terms which are well conserved in nMDS results (Fig. 1). This causes lack of potentially promoter motif and enhanced GO terms in G2 phase[2]. This means, we had better to employ nMDS instead of sinusoidal fittings for the analysis of cell division cycle microarray experiments.

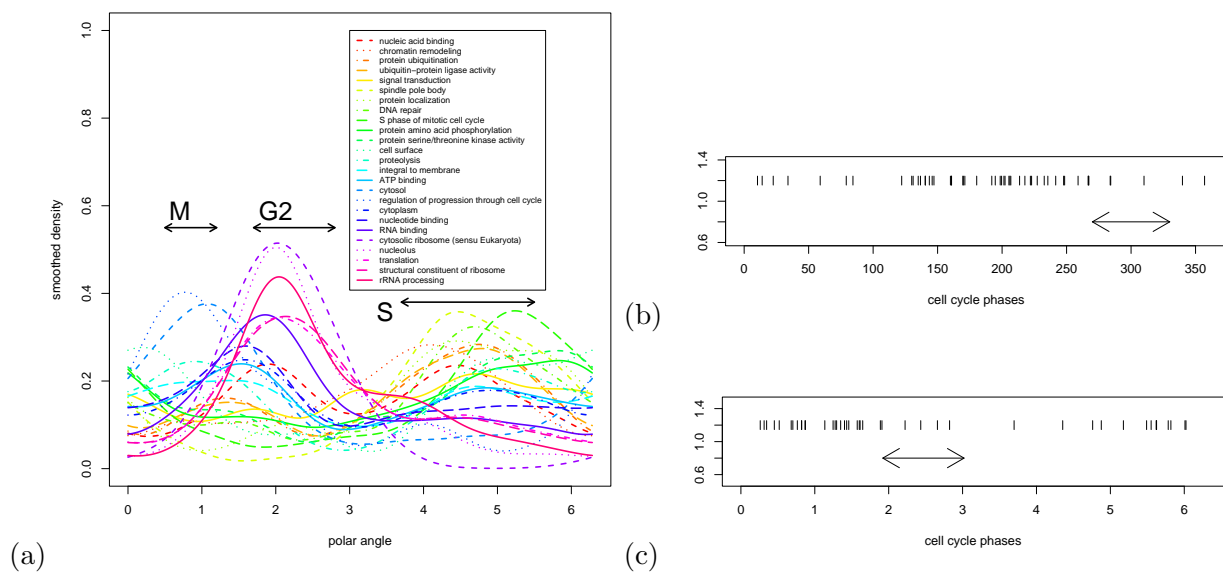


Figure 1: (a) Smoothed Distributions of genes associated with most frequent 50 GO terms along polar angle obtained by nMDS for Rustici et al's Elutriation 1 experiment[3], (b) Short vertical segments indicate the location of genes associated with GO term of "S phase of mitotic cell cycle" along cell cycle obtained by sinusoidal fittings for Oliva et al's Elutriation A experiment[1], and (c) the same as (b) for Peng et al's Elutriation 1 experiments[2]. The horizontal arrows in Figs. (b) and (c) indicated the period estimated as S phase based upon experimental observation of cell division process.

References

- [1] Oliva, A., Rosebrock, A., Ferrezuelo, F., Pyne, S., Chen, H., Futcher, B., and Leathwood, J., The Cell Cycle-Regulated Genes of *Schizosaccharomyces pombe*, *PLoS Biology* 3:e225, 2005.
- [2] Peng, X., Karuturi, K. M., Miller L., D., Lin, K., Yonghui, J., Kondu, P., Wang, L., Wong, L., Tak-Bun, L. E., Balasubramanian, M., and Jian-Hua, L., Identification of cell cycle-regulated genes in fission yeast, *Mol. Biol. Cell*, 16:1026–1042, 2005.
- [3] Rustici, G., Mata, J., Kivinen, K., Lió, P., Penkett, C. J., Burns, G., Hayles, J., Brazma, A., Nurse, P., and Bähler, J., Periodic gene expression program of the fission yeast cell cycle, *Nature Genetics* 36:809–817, 2004.
- [4] Taguchi, Y-h., Detecting Cell Cycle Regulated Genes of *Schizosaccharomyces pombe* by using Non-metric multidimensional scaling without sinusoidal fitting, *IPSI SIG Technical Report*, 2005-BIO-3:59–66, 2005.
- [5] Taguchi, Y-h., and Oono, Y., Nonmetric Multidimensional Scaling as a data-mining tool: new algorithm and new targets, *Advances in Chemical Physics*, 130B:315–351, 2005.
- [6] Taguchi, Y-h., and Oono, Y., Relational patterns of gene expression via non-metric multidimensional scaling analysis, *Bioinformatics*, 21(6):730–740, 2005.