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Poster presentation

Towards a mathematical model of the cAMP pathway in *S. cerevisiae*

Thomas Williamson*[1], Frank Bruggemann[2], Douglas Kell[2] and Lubomira Stateva[1]

Address: [1]Faculty of Life Scienes, Michael Smith Building, Univeristy of Manchester, Manchester, UK and [2]Manchester Interdisciplinary Biocentre, University of Manchester, Manchester, UK

Email: Thomas Williamson* - thomas.williamson@postgrad.manchester.ac.uk

* Corresponding author

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Background

The small, diffusible molecule cAMP plays a key signalling role in almost all organisms. In *S. cerevisiae*, cAMP is synthesized by adenylate cyclase [1], and hydrolyzed by the phosphodiesterases Pde1p and Pde2p [2,3]. The only function of cAMP in yeast is to activate PKA (Protein Kinase A). A molecule of PKA is a tetramer consisting of two catalytic (C) and two regulatory (R) subunits. Cyclic AMP binds to the R subunit, allowing its dissociation from C, allowing C to become catalytically active. PKA is believed to activate Pde1p [4], as well as indirectly inhibit the activity of adenylate cyclase [5]. We have created two mathematical models (one simplified and one detailed) in order to better understand the mechanisms of PKA activation. We have also created a model to investigate the complete cAMP pathway.

Results

The PKA models are able to behave appropriately when the cAMP level is altered, giving an increased concentra-

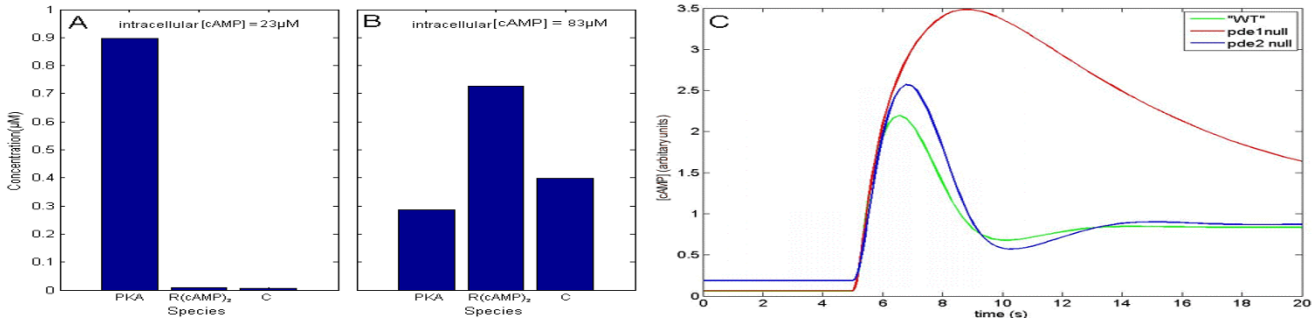

Figure 1
Species concentrations of the detailed PKA model under low (A) and high (B) cAMP concentration. C: cAMP levels of model mutants. Glucose concentration is increased after five seconds.

tion of free catalytic subunit (see Figure 1). In the wild type complete pathway model a "spike" of cAMP is observed after glucose addition. The cAMP level oscillates before reaching a steady state. The spike has a higher peak in the *pde1Δ* mutant (see Figure 1).

Conclusion

The models of PKA activation can reproduce events seen *in vivo*, but the detailed model also allows for concentrations of intermediates to be predicted. This could give insights into the mechanism by which PKA activation is regulated. The complete pathway model can reproduce phosphodiesterase knockout mutant phenotypes seen *in vivo* [4], as well as predicting that the cAMP level oscillates before reaching a steady-state. Further analysis and development of these models should give further insights into the cAMP pathway in yeast.

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