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TRACKING TRENDS & PERFORMANCE IN BASIC RESEARCH

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2009 : December 2009 - Emerging Research Fronts : Michael R.H. White on the Dynamics of Gene Expression

## EMERGING RESEARCH FRONTS - 2009

December 2009



Michael R.H. White talks with *ScienceWatch.com* and answers a few questions about this month's Emerging Research Front Paper in the field of Biology & Biochemistry.



**Article: Oscillations in NF-kappa B signaling control the dynamics of gene expression**

Authors: Nelson, DE, et al.

Journal: SCIENCE, 306 (5696): 704-708 OCT 22 2004

Addresses: Ctr Cell Imaging, Sch Biol Sci, Biosci Res Bldg, Crown St, Liverpool L69 7ZB, Merseyside, England.

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(addresses have been truncated.)

### SW: Why do you think your paper is highly cited?

This paper was the first experimental description of NF- $\kappa$ B oscillations in single cells. This represented a new way of thinking about this well-studied pathway. We also provided direct evidence that continuation of the oscillations also resulted in maintenance of gene expression. The paper included the application of a mathematical model to study the system. This has been recognized as a leading example of predictive systems biology.

### SW: Does it describe a new discovery, methodology, or synthesis of knowledge?

Yes, the study used state-of-the-art cell imaging to show a process that for most people was entirely unexpected. A further key attribute was that it was a systems biology study that involved both mathematical and experimental analyses.

### SW: Would you summarize the significance of your paper in layman's terms?

It has often been assumed that signaling through NF- $\kappa$ B may depend simply on the amount of NF- $\kappa$ B that enters the nucleus. This can be described in terms of "amplitude" or the control can be described as being obtained through "amplitude modulation (AM)."

We found that NF- $\kappa$ B, rather like calcium signaling, shows oscillatory behavior. It has long been shown that calcium signaling can carry information in the timing between the peaks. This can be described in terms of "frequency" or the control can be described as being through "frequency modulation (FM)."

Our results in the Nelson *et al.*, paper suggested that NF- $\kappa$ B had the potential characteristics of a protein-based signaling system that might use frequency

modulation to carry information. Our recent paper in *Science* by L. Ashall, *et al.*, "Pulsatile stimulation determines timing and specificity of NF- $\kappa$ B-dependent transcription," *Science* 10(324):

242-6, April 10, 2009, has provided direct evidence for this hypothesis.

**SW: How did you become involved in this research and were any particular problems encountered along the way?**

The research arose from an initial collaboration with AstraZeneca. The key problems lay in establishing the long-term microscopy experiments which became possible when we moved to temperature controlled rooms in a new building.

**SW: Where do you see your research leading in the future?**

The paper has recently led on to a further paper in *Science* (as noted above) where we have provided direct experimental evidence that the frequency of oscillations does indeed control which genes are switched on. We have also used mathematical models to predict the source and perhaps a role for heterogeneity in the timing of the oscillations between cells.

Overall, this work is relevant for understanding the propagation and resolution of inflammation in cells and tissues. At the same time, the principles that lie behind the mechanism of action of this system might also be relevant to understanding other signaling systems.

**SW: Do you foresee any social or political implications for your research?**

In the long term, our new understanding of this system may allow for the development of new types of treatments for inflammatory disease.

**Professor Michael R.H. White, Ph.D.**

**School of Biological Sciences**

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**Web**

KEYWORDS: P65 SUBUNIT; TRANSCRIPTION; ALPHA; CELLS; PHOSPHORYLATION; ACTIVATION; TIME; ACETYLATION; MECHANISMS; SERINE-536.

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