Convergence of Transcription, Metabolomics and Wireless Nano-Sensor Networks

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Gene Expression: Regulation of Transcription

DNA sequence-specific transcription factors

Eukaryotic promoter

TFIID

pol II

mRNA

Exons

TBP (TATA-binding protein)
Transcription Unit

- Promoter
- Transcribed region
- Transcription start site
- Termination signals
- Coding strand 5’
- Template strand 3’
- -35 region
- -10 region
- PPP
- OH
- 5’ Flanking sequences
- 3’ Flanking sequences

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Initiation Complex: RNA Polymerase II
Initiation Complex: TATA Binding Protein
Initiation Complex: TATA Binding Protein
TFIID – TBP : TATA Binding Protein

PROLINE $\left(\beta_1\right)_{50}^{y,h}$

LEUCINE $\left(\beta_1\right)_{50}^{Pf}$

$y \rightarrow$ Saccharomyces cerevisiae; $h \rightarrow$ humans; Pf $\rightarrow$ Plasmodium falciparum
TBP: Yeast, humans and malaria parasite

PROLINE \((\beta_1)^{y,h}_{50}\)

LEUCINE \((\beta_1)^{Pf}_{50}\)

Pol II, Pol III

Pol I – VSG

http://dspace.mit.edu/handle/1721.1/41898
Initiation Complex: RNA Polymerase II
Eukaryotic RNA Polymerase II Subunits

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RNA Polymerase II Subunit 1: RPB1

C Terminal Domain (CTD): \([\text{YSPTSPS}]_n\)

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<tbody>
<tr>
<td><img src="image1.png" alt="Chemical Structure of TYR" /></td>
<td><img src="image2.png" alt="Chemical Structure of SER" /></td>
<td><img src="image3.png" alt="Chemical Structure of PRO" /></td>
<td><img src="image4.png" alt="Chemical Structure of THR" /></td>
<td><img src="image5.png" alt="Chemical Structure of SER" /></td>
<td><img src="image6.png" alt="Chemical Structure of PRO" /></td>
<td><img src="image7.png" alt="Chemical Structure of SER" /></td>
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RNA Polymerase II Subunit 1: RPB1 C Terminal Domain (CTD): [YSPTSPS]_n

\[
\begin{array}{cccccc}
\text{TYR} & \text{SER} & \text{PRO} & \text{THR} & \text{SER} & \text{PRO} & \text{SER} \\
[\text{Y}] & [\text{S}] & [\text{P}] & [\text{T}] & [\text{S}] & [\text{P}] & [\text{S}] \\
\end{array}
\]
RNA Polymerase II Subunit 1: RPB1

C Terminal Domain (CTD): [YSPTSPS]_n

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Yeast

\( y_{RPB1\text{-CTD}}: [YSPTSPS]_{26} \)

Human

\( h_{RPB1\text{-CTD}}: [YSPTSPS]_{52} \)

Malaria

\( p_{RPB1\text{-CTD}}: [YSPTSPS]_{15} + 63 \text{ aa} \)

Trypanosome

\( t_{RPB1\text{-CTD}}: [YSPTSPS]_{0} \)
Host-Parasite Interactions: CTD

**Human**

hRPB1-CTD: [YSPTSPS]$_{52}$

**Malaria**

pRPB1-CTD: [YSPTSPS]$_{15}$ + 63 amino acids

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Host-Parasite Interactions
Unique CTD Proteins Regulating Malaria Gene Expression in Infected Humans

Human

hRPB1-CTD: [YSPTSPS]$_{52}$

Malaria

pRPB1-CTD: [YSPTSPS]$_{15}$ + 63 amino acids

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Identification of Targets for RNA Immunity?
Are Unique CTD Proteins Regulating Malaria Gene Expression in Infected Humans?

Malaria specific?
If target protein is specifically parasite induced: A Potential for Development of Malaria Therapy
Detection of Target Human Protein: Constitutive Expression ?
Early detection of infection by Malaria parasite *P. falciparum* ?

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Other Tools to Identify Unique Target Proteins: Mass Spec Analysis
Mass Spectrometric Analysis of Proteomes in Ovarian Cancer

Samples from unaffected individuals

Samples from cancer patients

Generate protein mass spectra (15,200 mass/charge values)

Genetic algorithm + self-organising cluster analysis

Discriminatory pattern: plot of relative abundance of 5–20 key proteins (mass/charge values) that best distinguish cancer from non-cancer

Mass/charge
Sensors: Not necessarily *in vivo*, Not necessarily nano

**Ring Sensors**

*Sokwoo Rhee, Ph.D. thesis, MIT*

[www.sokwoo.com](http://www.sokwoo.com)
(a) Heart Rate (beats/min) by Electrocardiogram (ECG)

(b) Heart Rate (beats/min) by Fingertip Photoplethysmograph (PPG)

(c) Heart Rate (beats/min) monitored by Wireless Ring Sensor shown in Figure
Prime Target for Sensor-based Early detection & RNA-based Immunity
NanoCom: in vivo
Wireless Sensor Networks?

Multiple Variables
Homeostasis
Nash Equilibrium?
Data ...
More data points ...
Data shows emerging pattern...
Data: Young’s Double Slit Experiment with Electrons
Dr. Akira Tonomura, Hitachi Research Laboratories, JP
Directed Graph: Today’s Network
Social Networking
n = 10; p = 1,000
10 locations
1,000 lags

Estimate Coefficients:

10,000 \( \Phi \)
+ 10,000 for x’s = 20,000 per stage or 200,000 for n=10 (excluding constants and error coefficients)

\[
\begin{align*}
y_{1t} &= \beta_0 + \sum_{k=1}^{K} \sum_{i=1}^{N_{x_{kt}}} \alpha_{ki} x_{kt-i} + \phi_{11} y_{1t-1} + \phi_{12} y_{2t-1} + \epsilon_{1t} \\
y_{2t} &= \beta_0 + \sum_{k=1}^{K} \sum_{i=1}^{N_{x_{kt}}} \alpha_{ki} x_{kt-i} + \phi_{21} y_{1t-1} + \phi_{22} y_{2t-1} + \epsilon_{2t}
\end{align*}
\]

\[
\begin{align*}
\sigma_{1t}^2 &= \theta_0 + \sum_{i=1}^{q} \theta_{i} \epsilon_{1t-i}^2 + \sum_{j=1}^{p} \tau_{j} \sigma_{1t-j}^2 \\
\sigma_{2t}^2 &= \theta_0 + \sum_{i=1}^{q} \theta_{i} \epsilon_{2t-i}^2 + \sum_{j=1}^{p} \tau_{j} \sigma_{2t-j}^2
\end{align*}
\]
Healthcare: 50 years notice still policy failures

www.populationeurope.org

51.2 14.1 16.7 6.9 12 5.5 -3 0 -25.

IR UK SE ES FR NL DE RU US

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PARADIGM SHIFT
Reduces Healthcare Cost & Improves Service
Data & Information Asymmetry: Isolated DDT Systems
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RFID Linked Biometrics & NanoRFID Linked Biometrics & Nano-sensor Netsensor Net

AGRMIA  
Patient Data Omics Data Genetic Risk

Glucose Nano-sensor Radio

HEALTHCARE MANAGEMENT

802.16a Grid
Glucose, O₂ → Glucose Oxidase → H₂O₂ → Conducting polymer → Gold nanoelectrode

VISIT CLINIC

802.11b WiFi 802.11g

Charles Townes
Bernard Lown
Yuan T Lee

Glenn T Seaborg
Shoumen Datta
Louis Brennan

Helene Langevin Joliot

Glenn T Seaborg
Shoumen Datta
Dudley Herschbach

Clive Granger Louis Brennan

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Clive Granger Louis Brennan
Conceptual Convergence and the Wealth of Nations

Adoption

Technology Introduced


1800 1825 1853 1913 1969 2025 2061 2081

Textile  Railway  Auto  Computer  Agents Grid, SL  Nanotech Hydrogen Fusion

Industrial Revolution

Knowledge Economy

Atoms  Physical World Model

Bits

Economic History from Norman Poire
“Did not entail being right all the time. It was rather to dare, to propose new ideas, and then to verify them and to know how to admit errors.”

Professor Pierre-Gilles de Gennes* (1932-2007) after receiving the 1991 Nobel Prize for Physics

* Died 18 May 2007
Support research ...  

“Research is four things: brains with which to think, eyes with which to see, machines with which to measure and fourth, money.”

Albert Szent-Gyorgyi de Nagyrolt  
Nobel Prize in Medicine (1937)