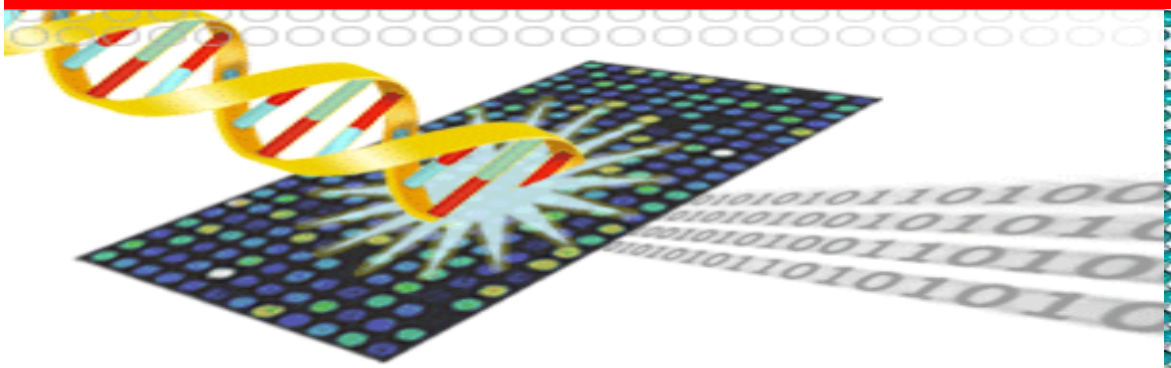
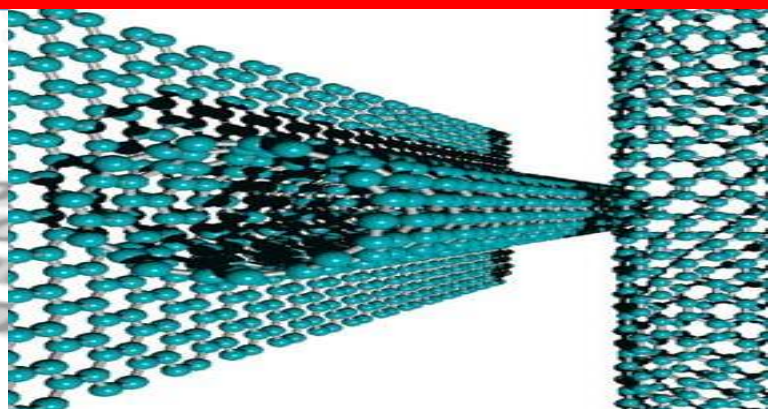
Convergence of Transcription, Metabolomics and Wireless Nano-Sensor Networks

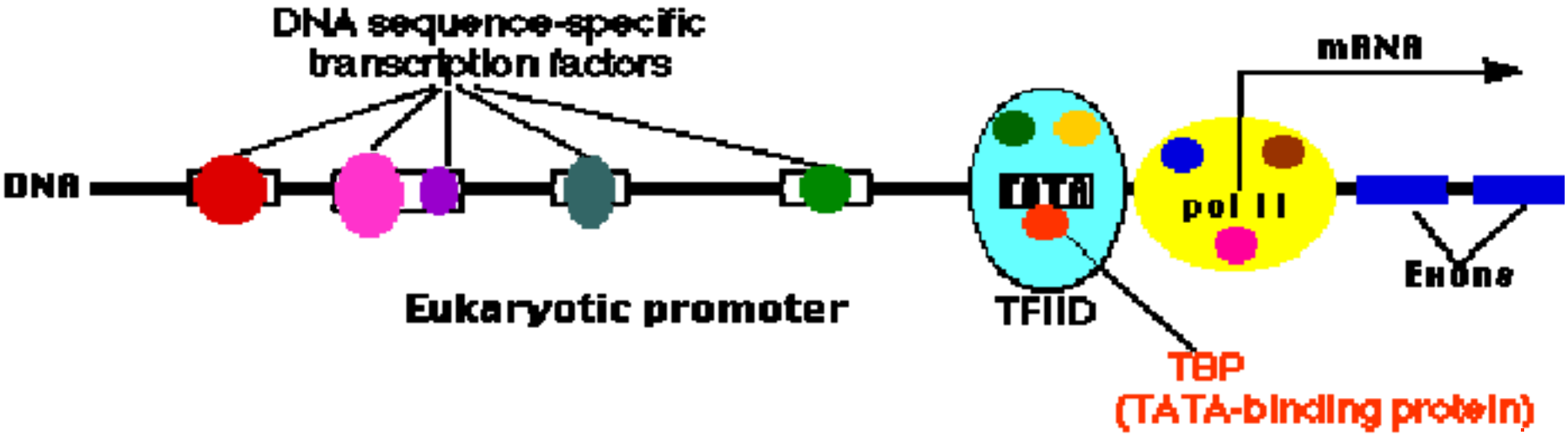
Shoumen Datta

Massachusetts Institute of Technology





Gene Expression: Regulation of Transcription



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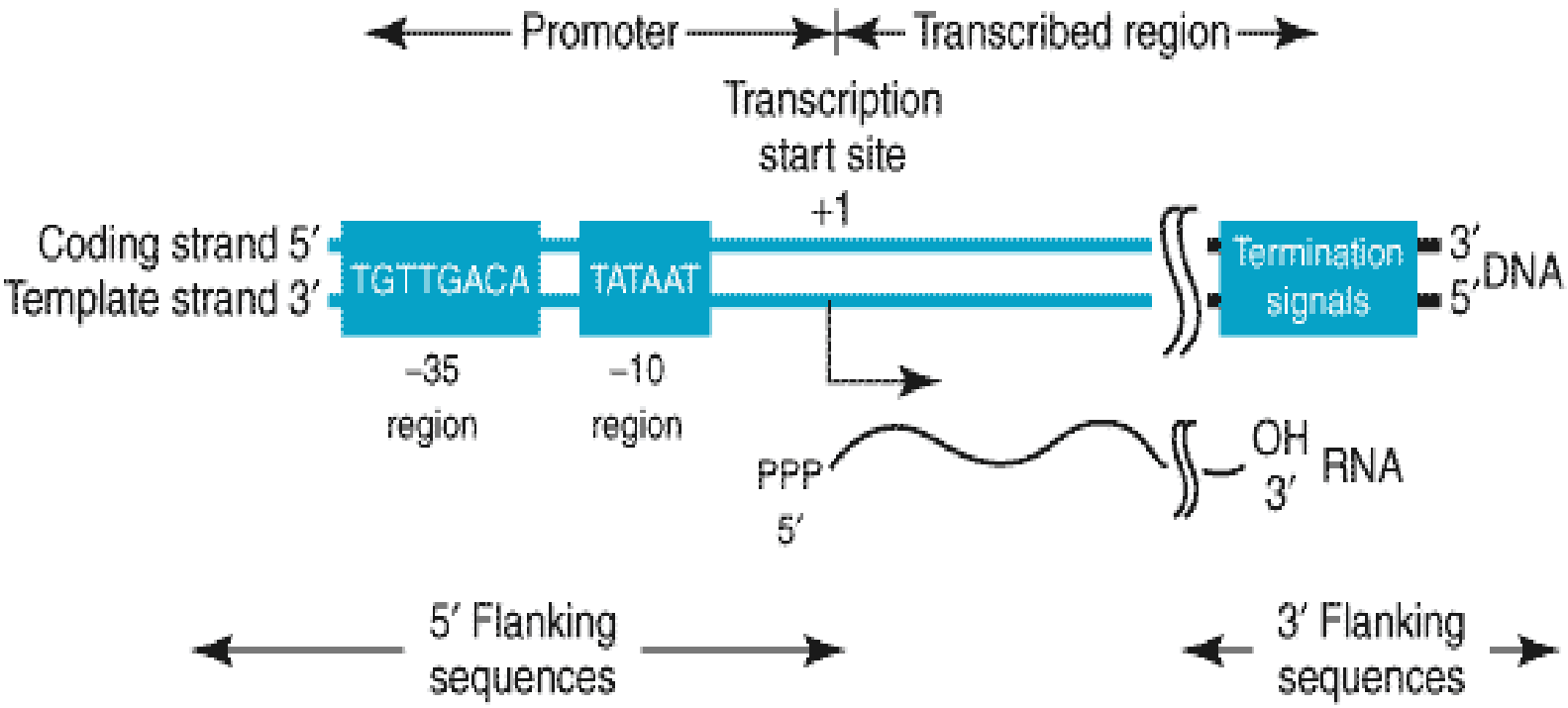
Transcription Unit



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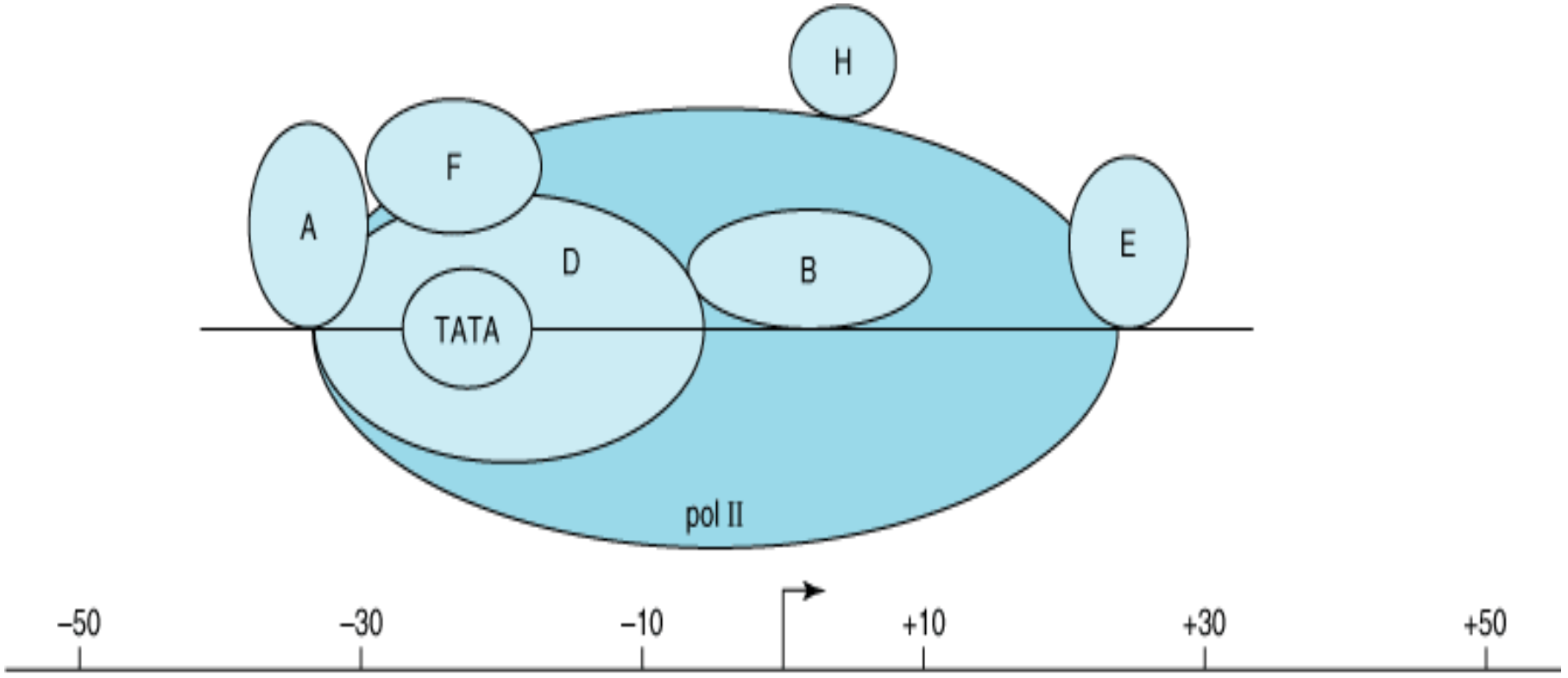
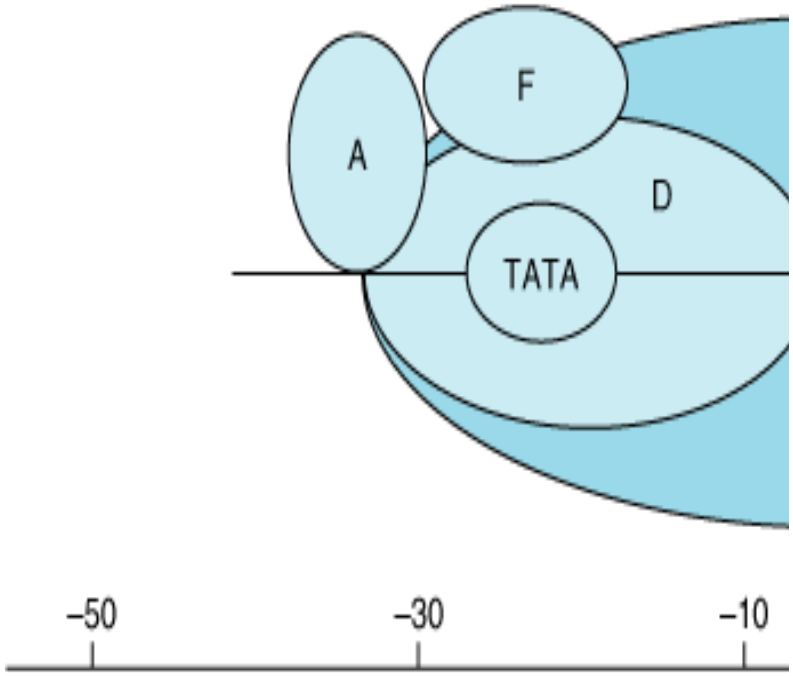
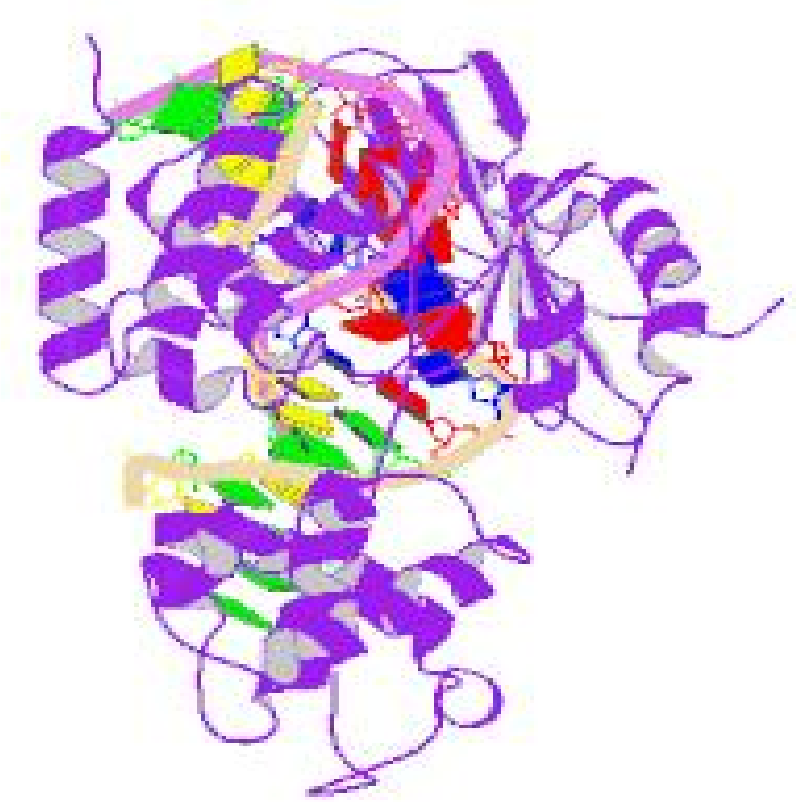
Initiation Complex: RNA Polymerase II



Initiation Complex: TATA Binding Protein





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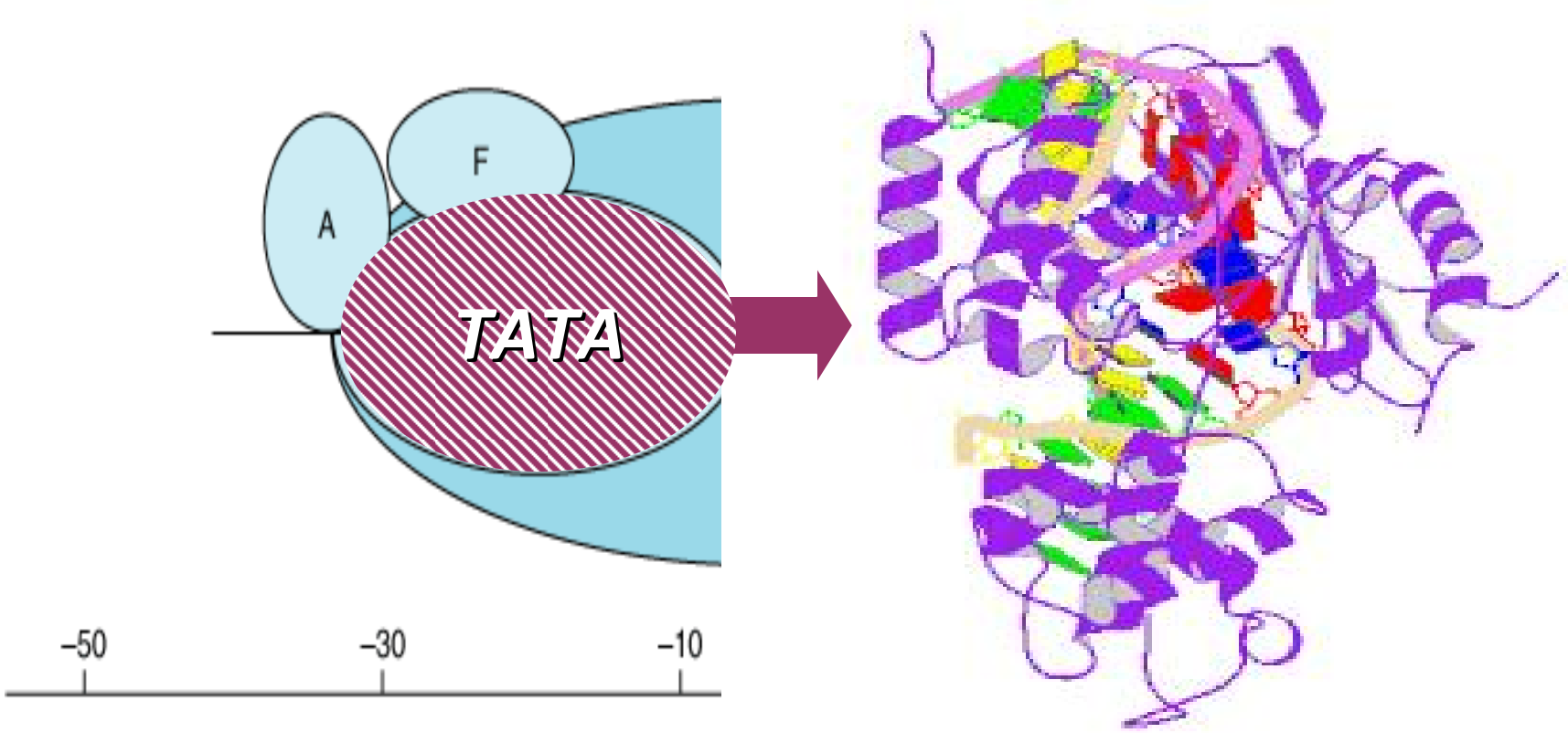
Initiation Complex: TATA Binding Protein



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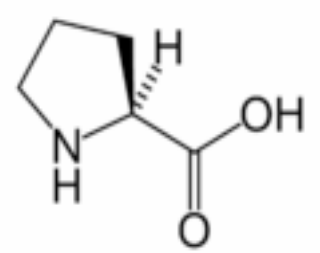
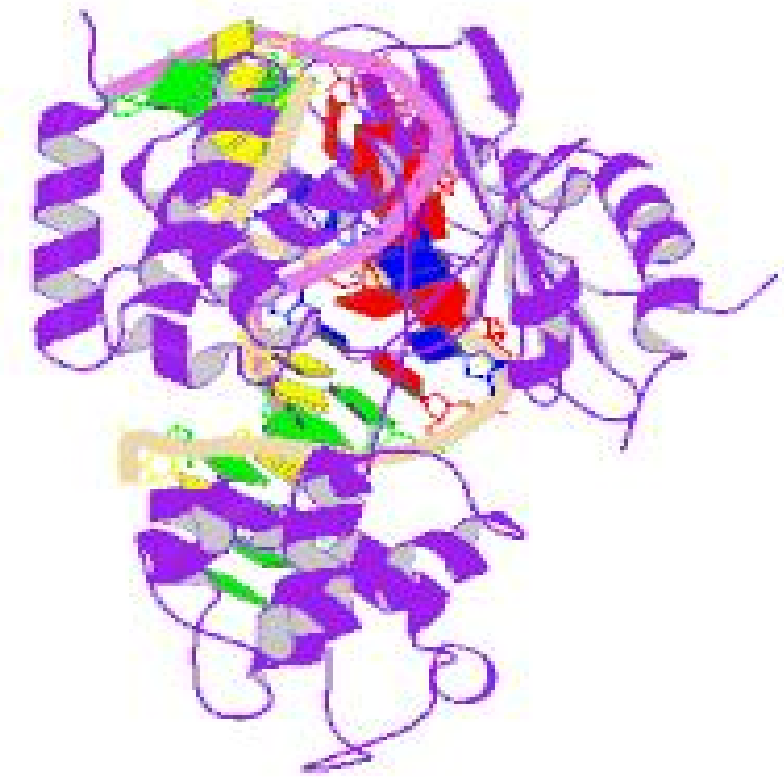
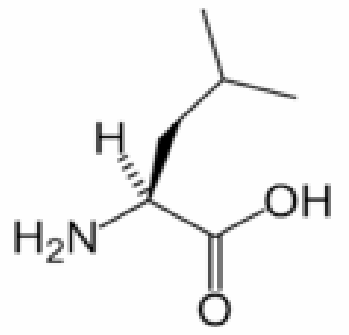
TFIID – TBP : TATA Binding Protein



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



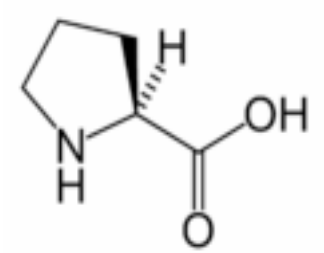


LEUCINE $(\beta_1)^{Pf}_{50}$

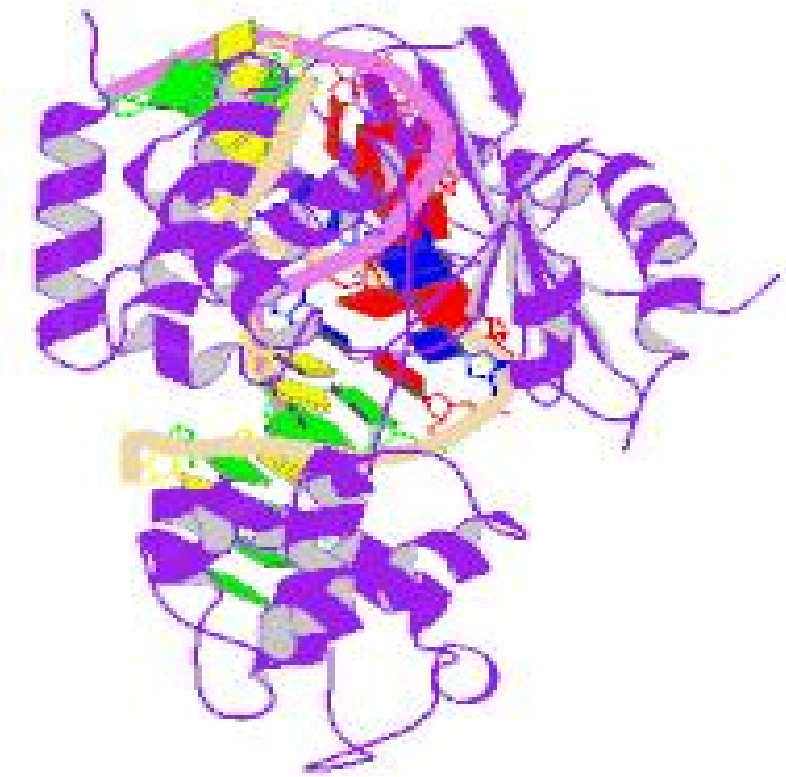
y → Saccharomyces cerevisiae; h → humans; Pf → Plasmodium falciparum

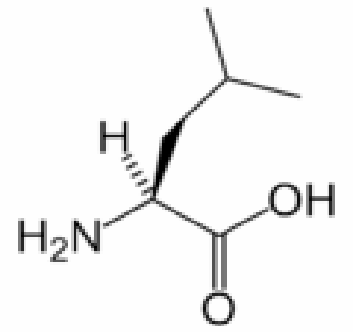
TBP: Yeast, humans and malaria parasite

Pol II, Pol III



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





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

Pol I – VSG

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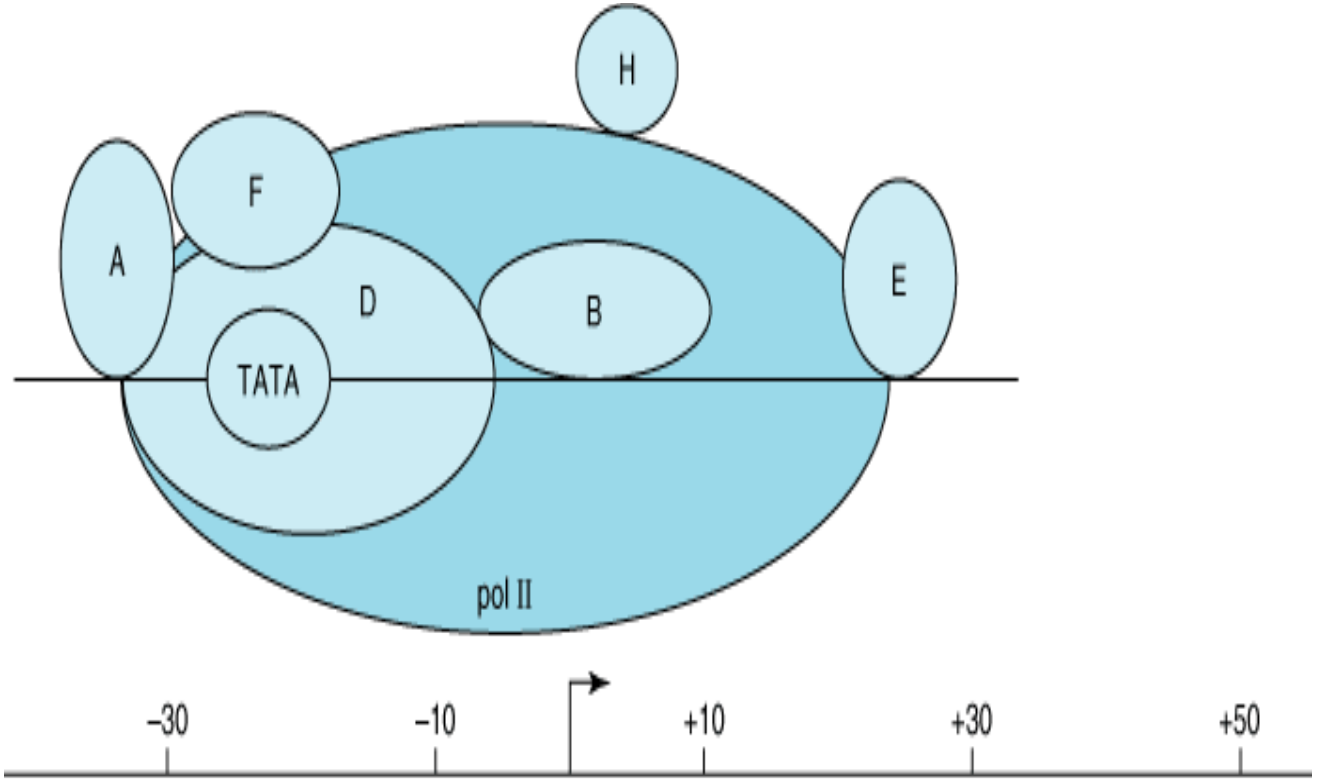
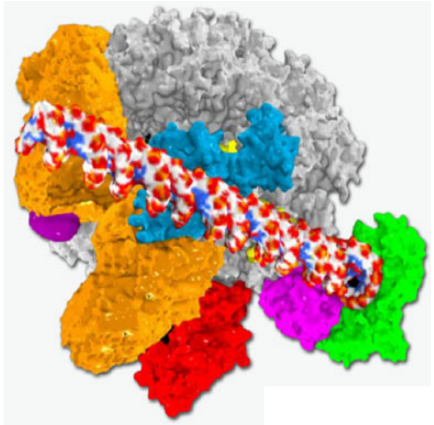
http://dspace.mit.edu/handle/1721.1/41898

Initiation Complex: RNA Polymerase II





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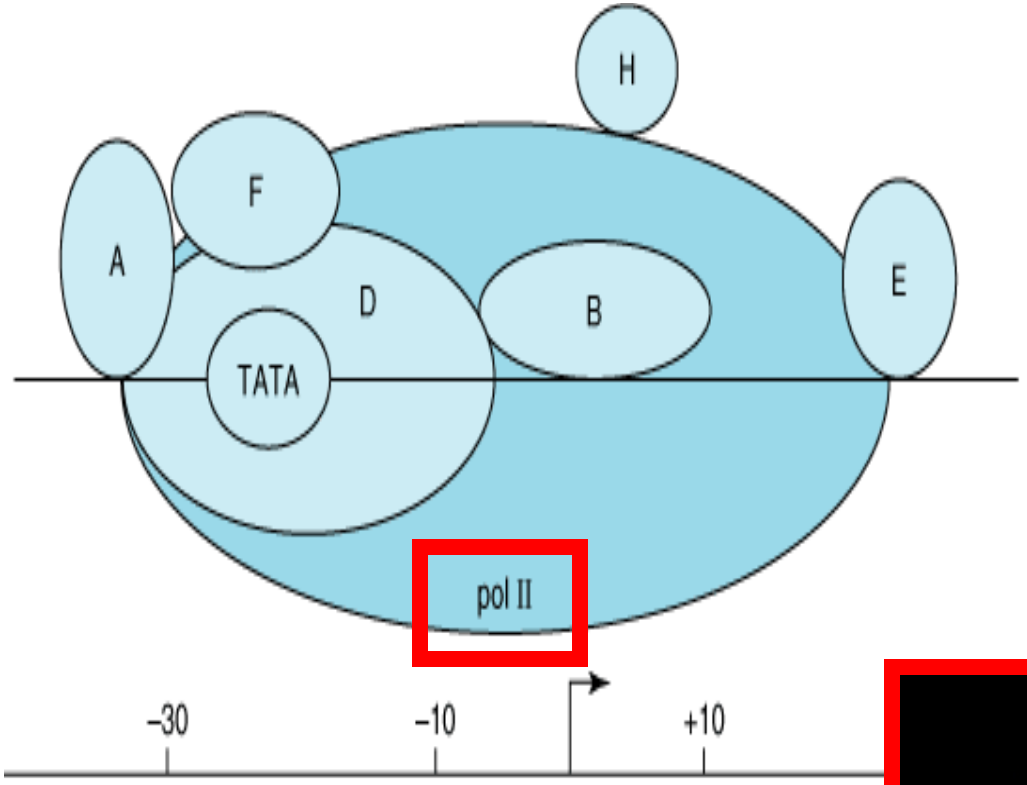
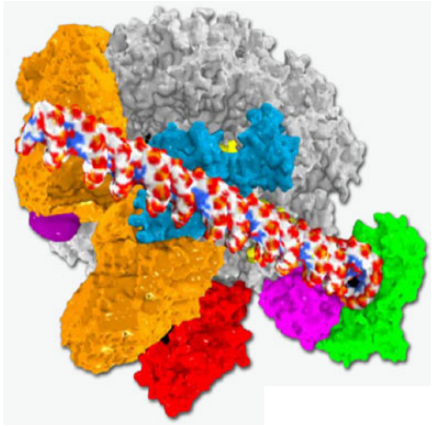
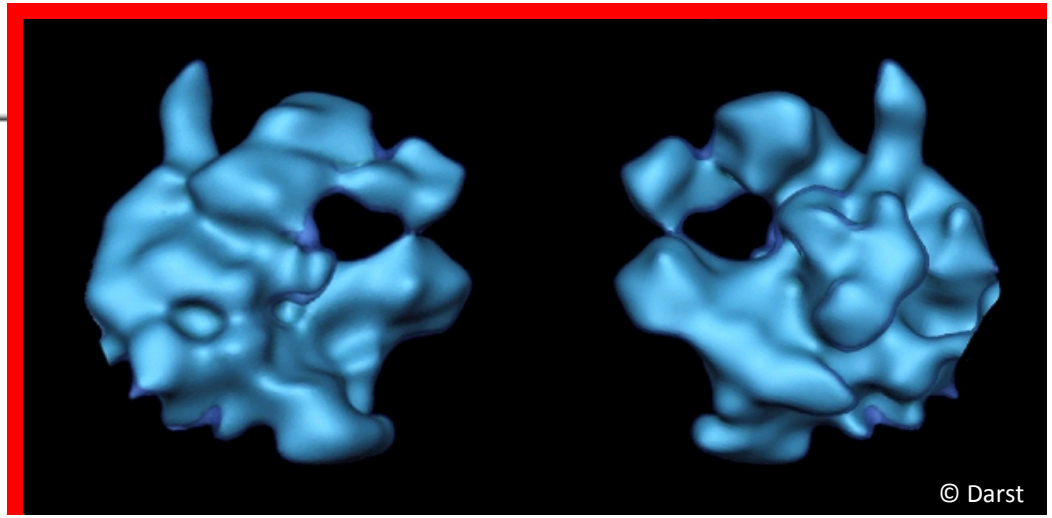
Eukaryotic RNA Polymerase II Subunits







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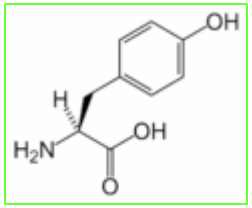
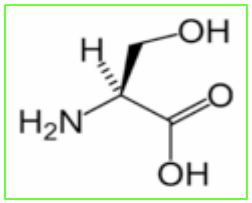
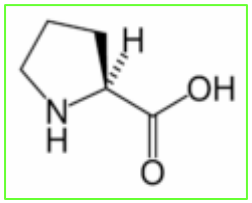
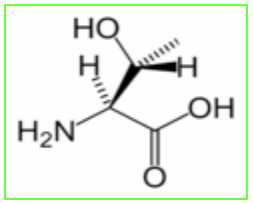
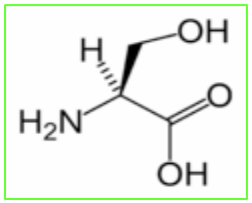
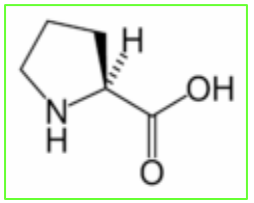
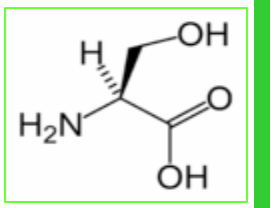
RNA Polymerase II Subunit 1 : RPB1
C Terminal Domain (CTD): $[YSPTSPS]_n$

TYR [Y]	SER [S]	PRO [P]	THR [T]	SER [S]	PRO [P]	SER [S]
						

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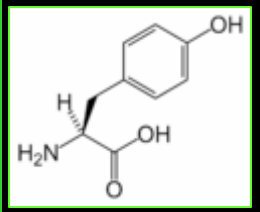
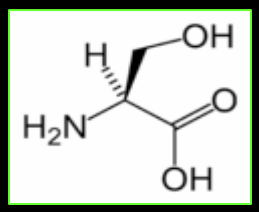
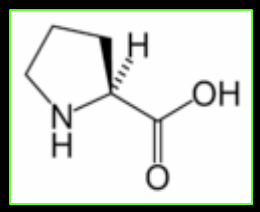
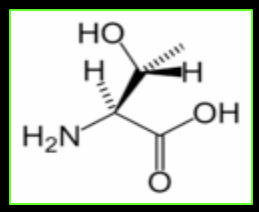
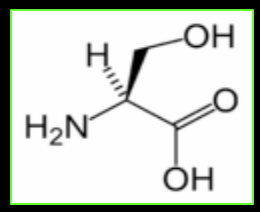
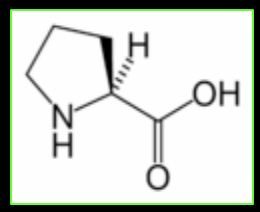
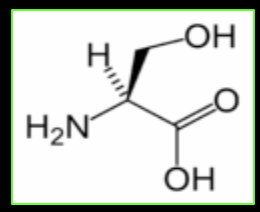
RNA Polymerase II Subunit 1 : RPB1
C Terminal Domain (CTD): $[YSPTSPS]_n$

TYR [Y]	SER [S]	PRO [P]	THR [T]	SER [S]	PRO [P]	SER [S]
						

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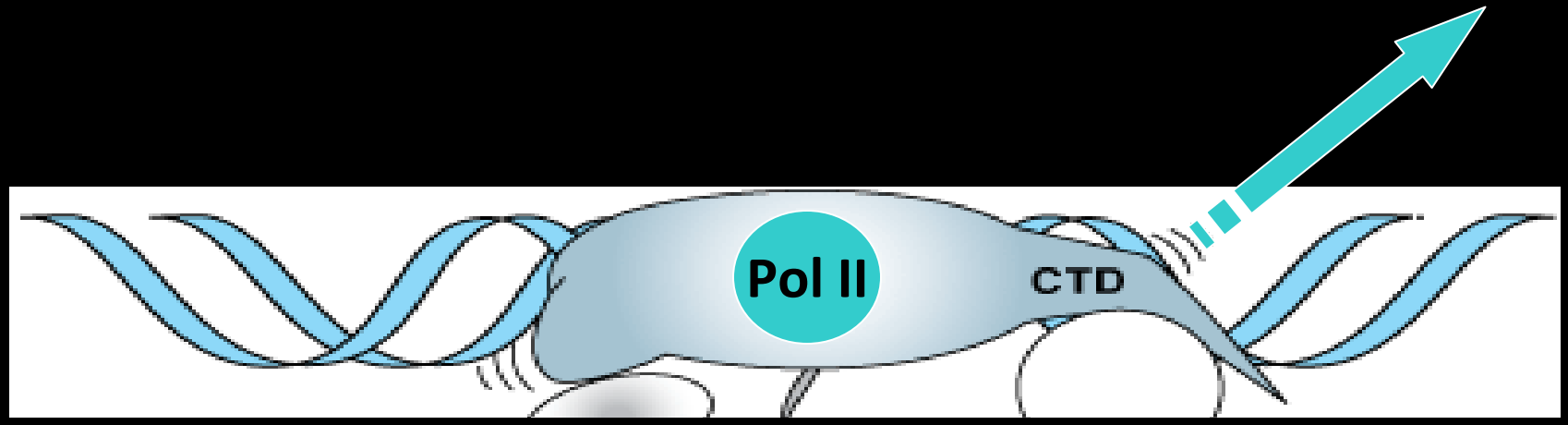
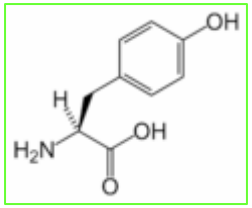
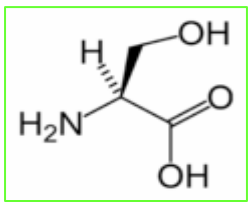
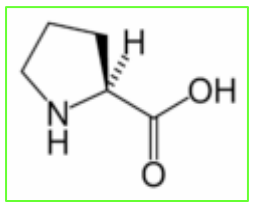
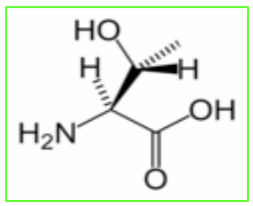
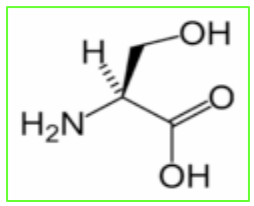
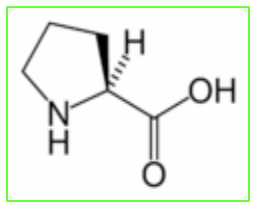
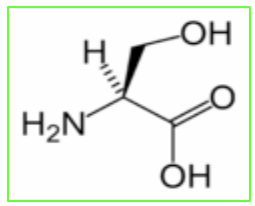


RNA Polymerase II Subunit 1 : RPB1
C Terminal Domain (CTD): $[YSPTSPS]_n$

TYR [Y]	SER [S]	PRO [P]	THR [T]	SER [S]	PRO [P]	SER [S]
						

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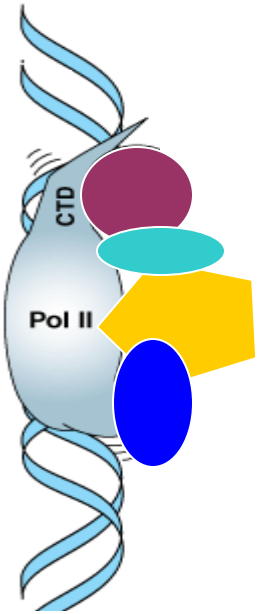
Yeast **yRPB1-CTD: $[YSPTSPS]_{26}$**

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

Malaria **pRPB1-CTD: $[YSPTSPS]_{15}$ + 63 aa**

Trypanosome **tRPB1-CTD: $[YSPTSPS]_{0}$**



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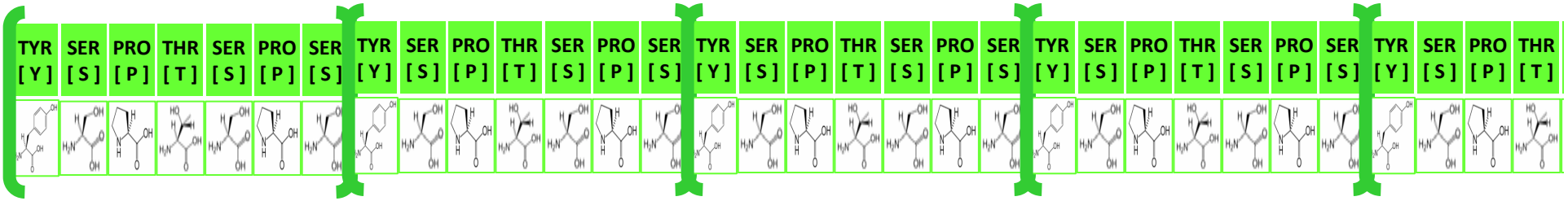
Host-Parasite Interactions: CTD

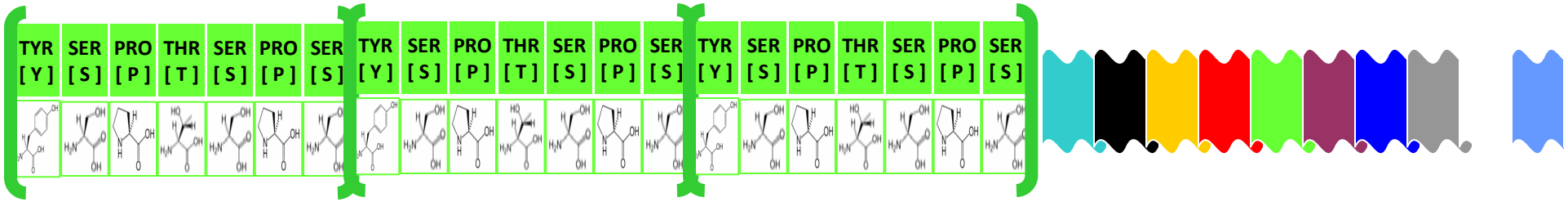
Human

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



Malaria

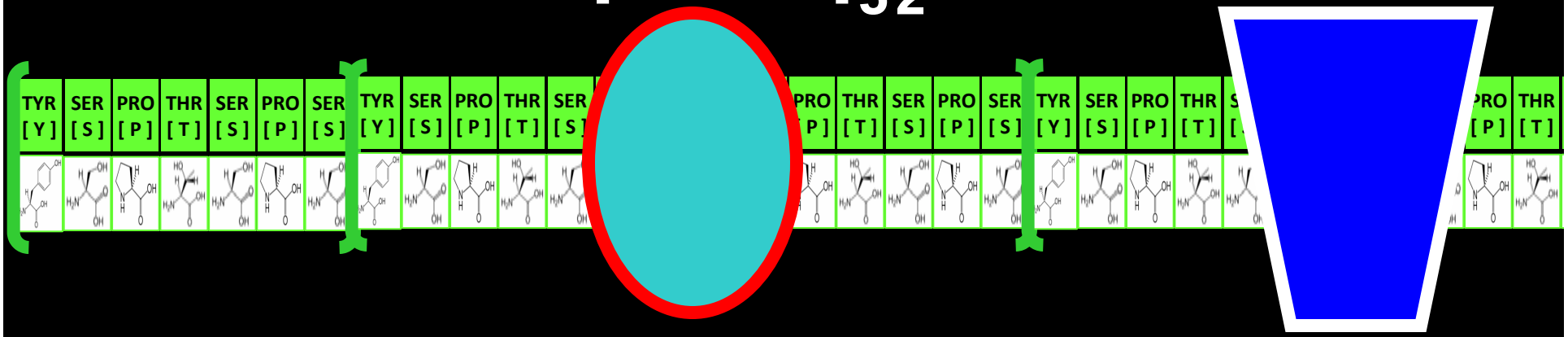
pRPB1-CTD: [YSPTSPS]$_{15}$ + 63 amino acids



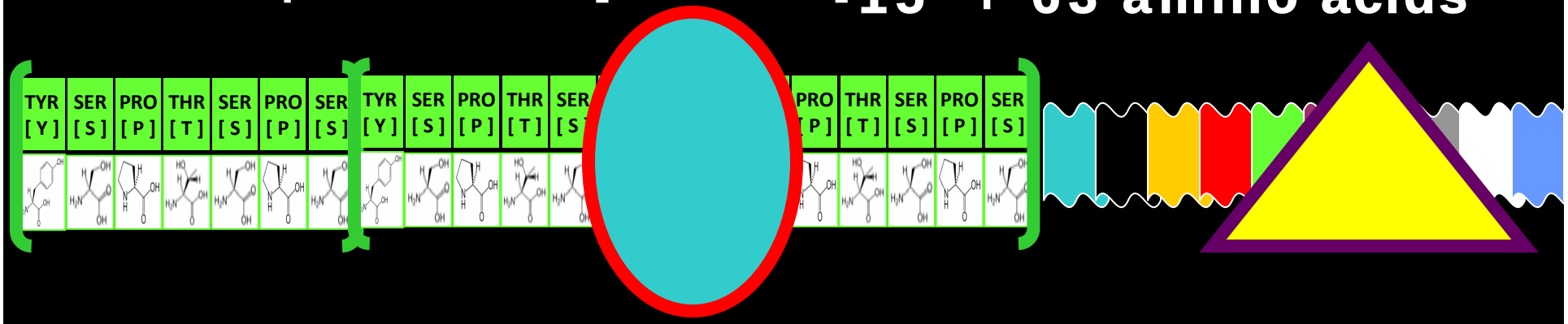
Host-Parasite Interactions

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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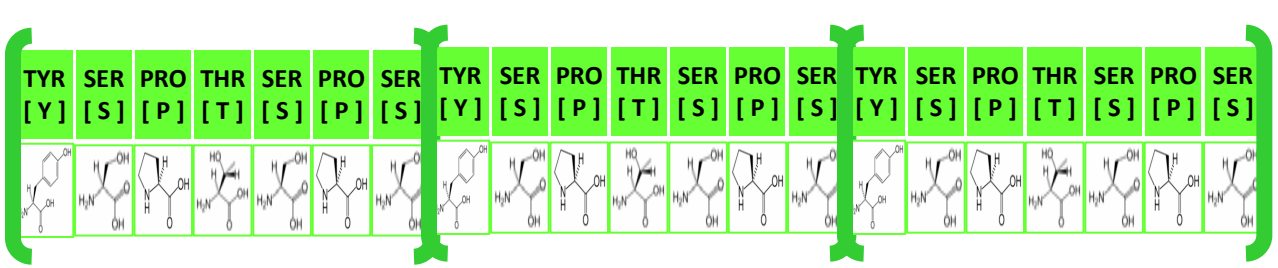
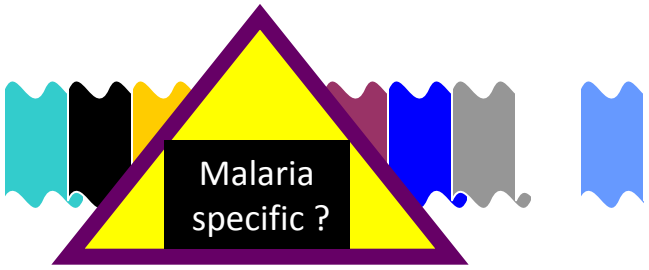
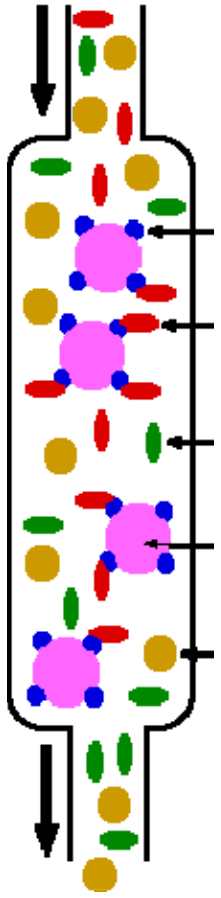
Identification of Targets for RNA Immunity ?

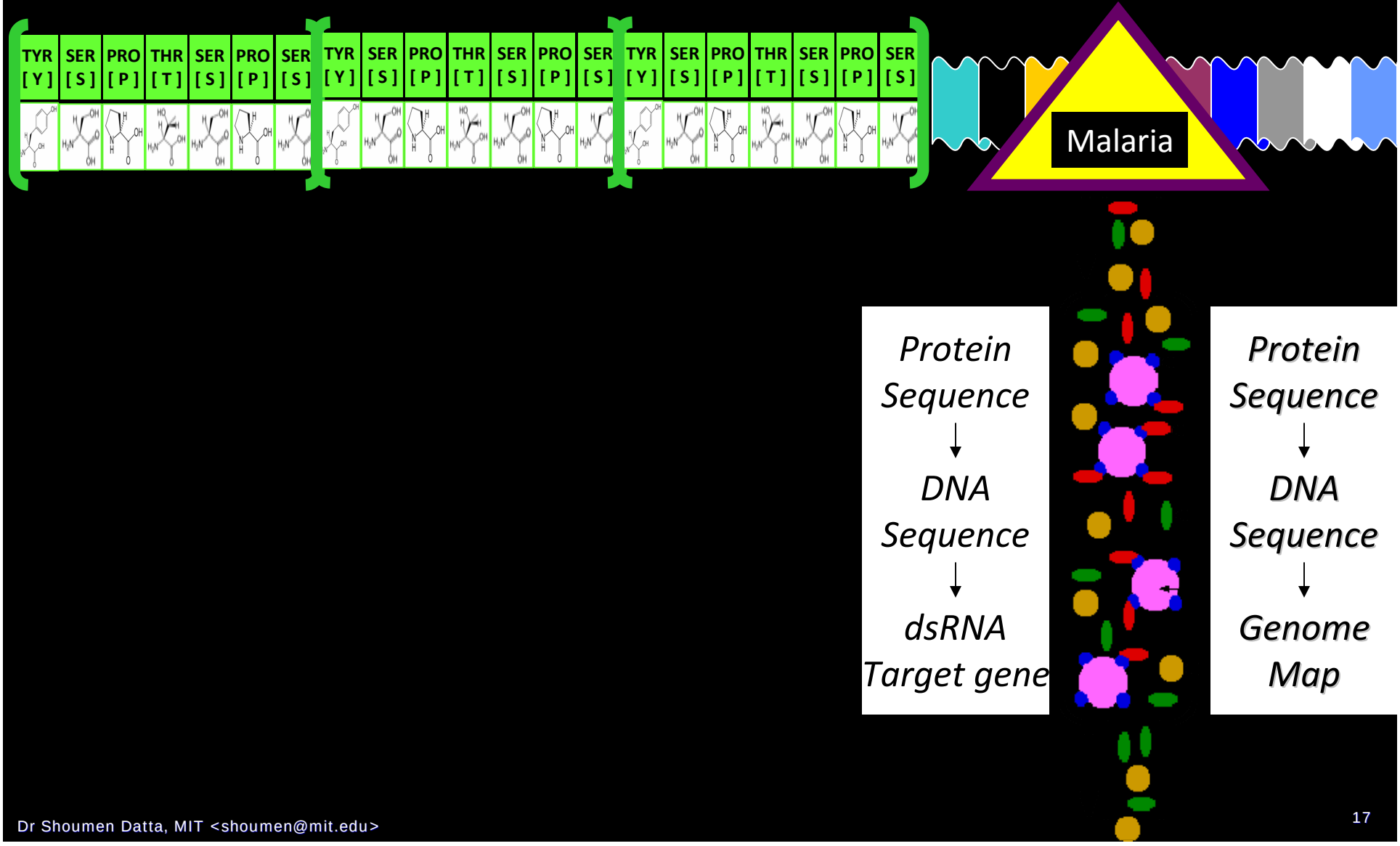
Are Unique CTD Proteins Regulating Malaria Gene Expression in Infected Humans ?



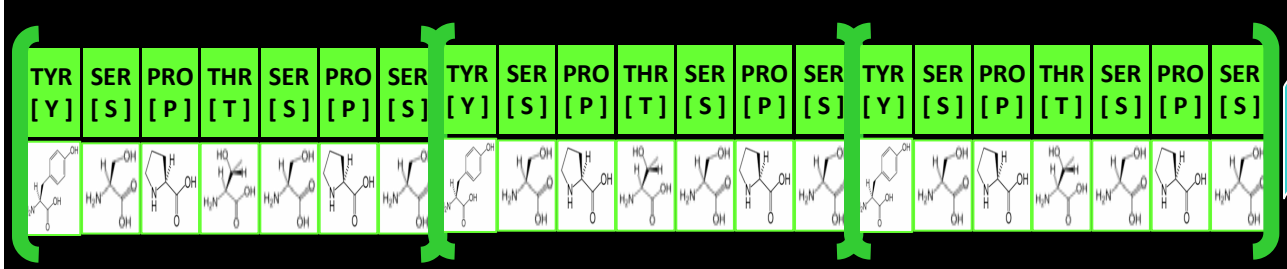


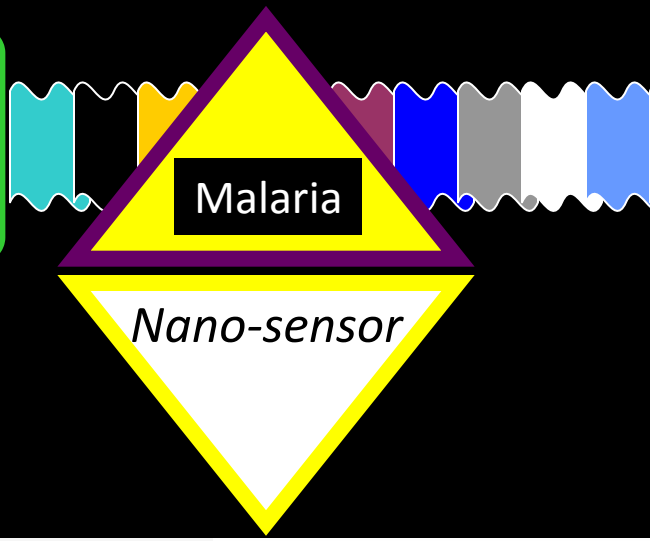


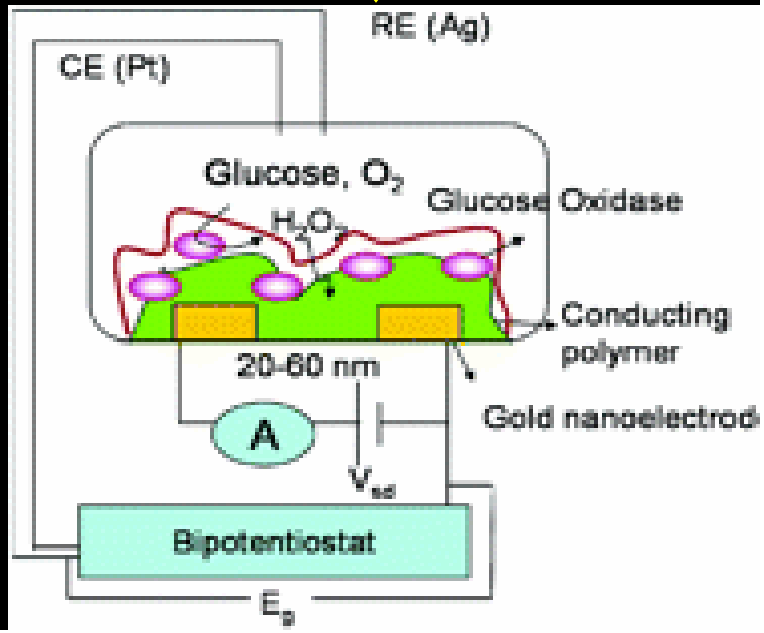
If target protein is specifically parasite induced: A Potential for Development of Malaria Therapy



Detection of Target Human Protein: Constitutive Expression ?
Early detection of infection by Malaria parasite *P. falciparum* ?







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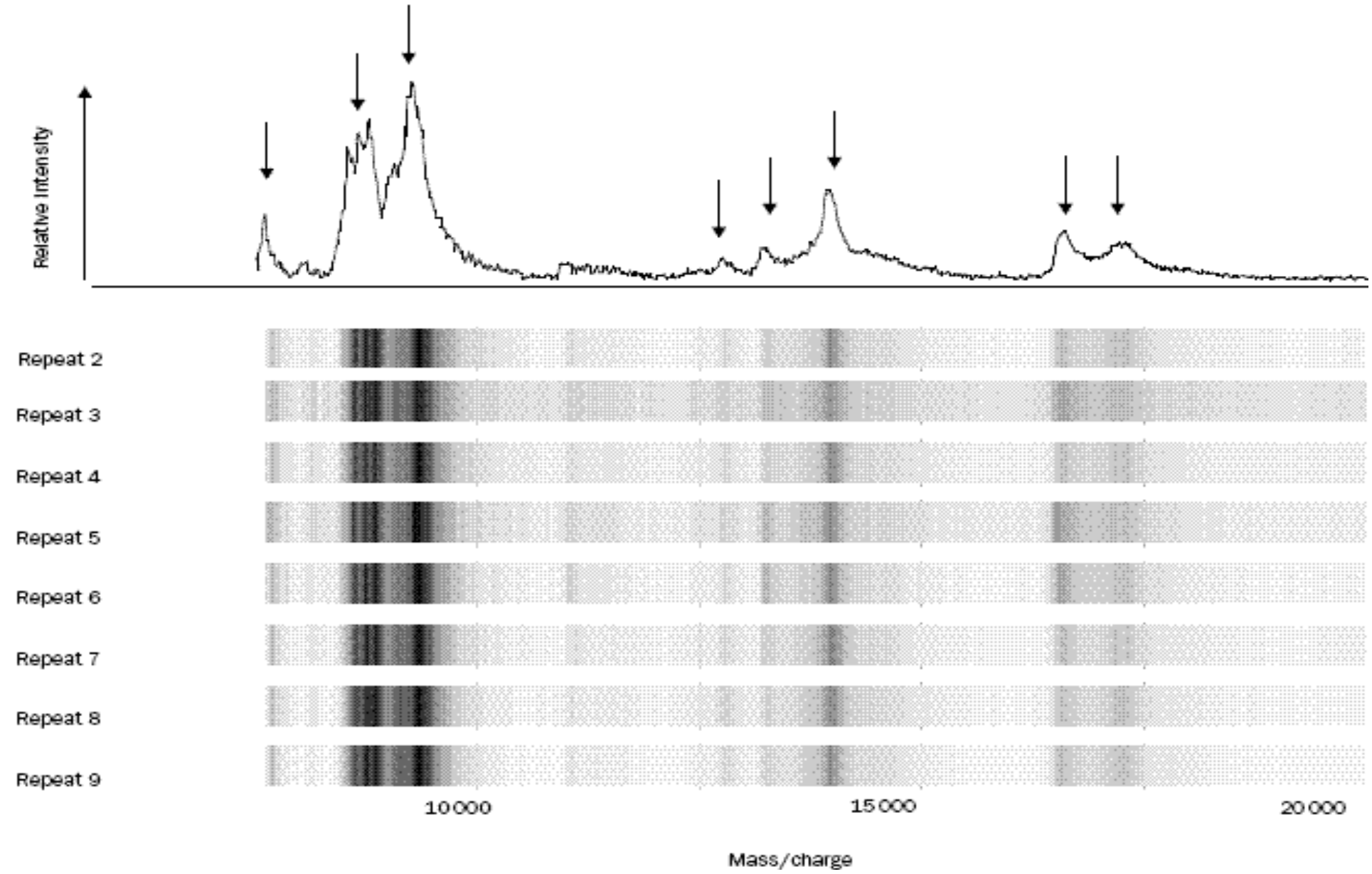
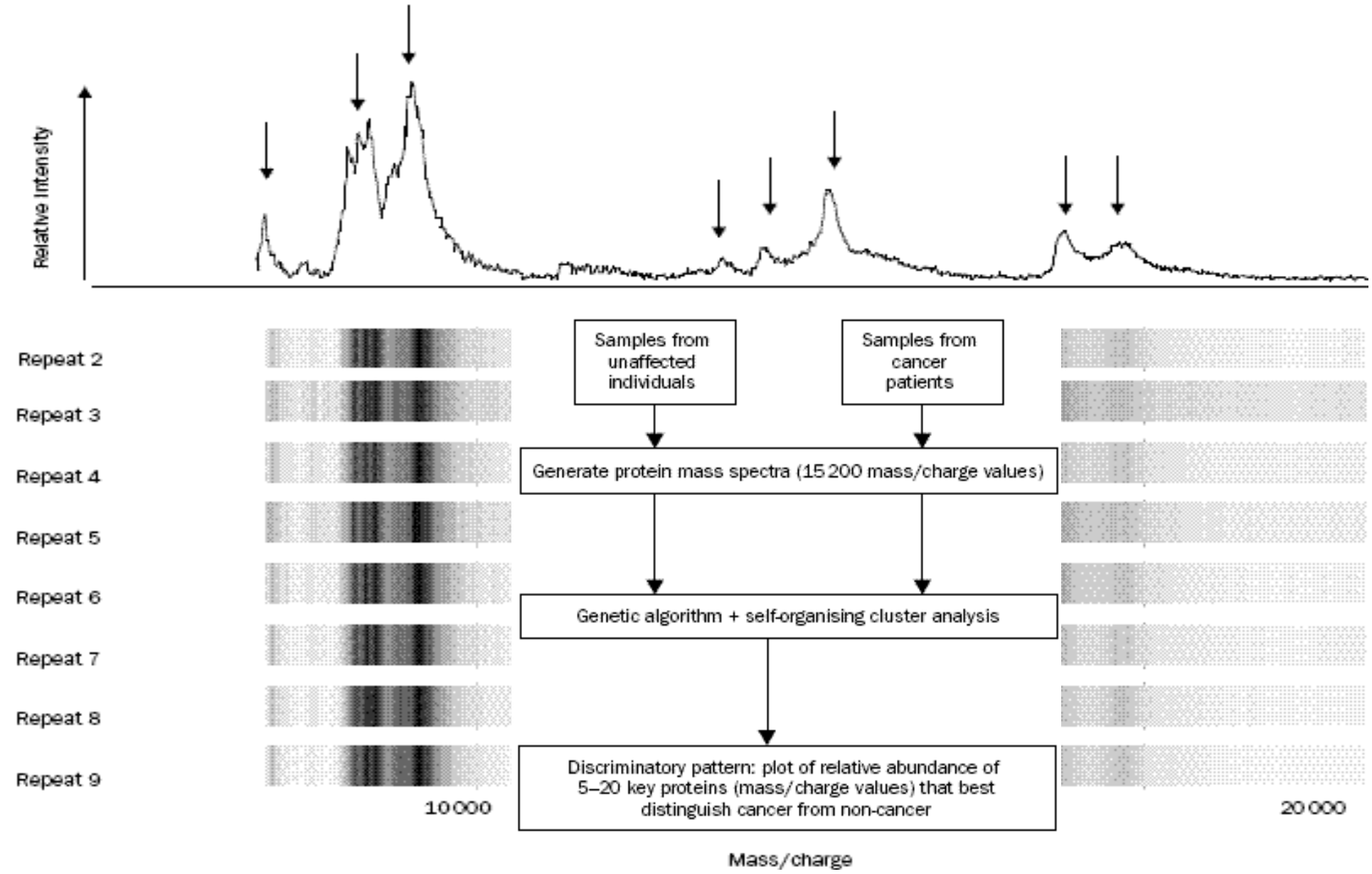
NanoLetters (2004) 4 1785-1788

Other Tools to Identify Unique Target Proteins: Mass Spec Analysis



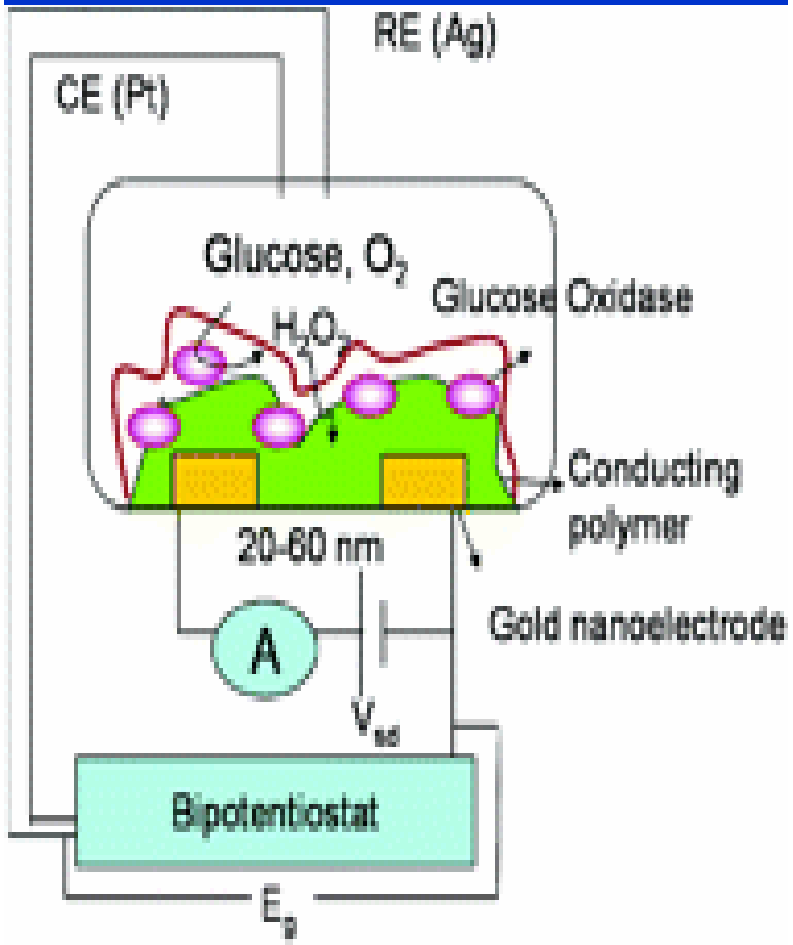
Mass Spectrometric Analysis of Proteomes in Ovarian Cancer

Lancet 2002 359 574



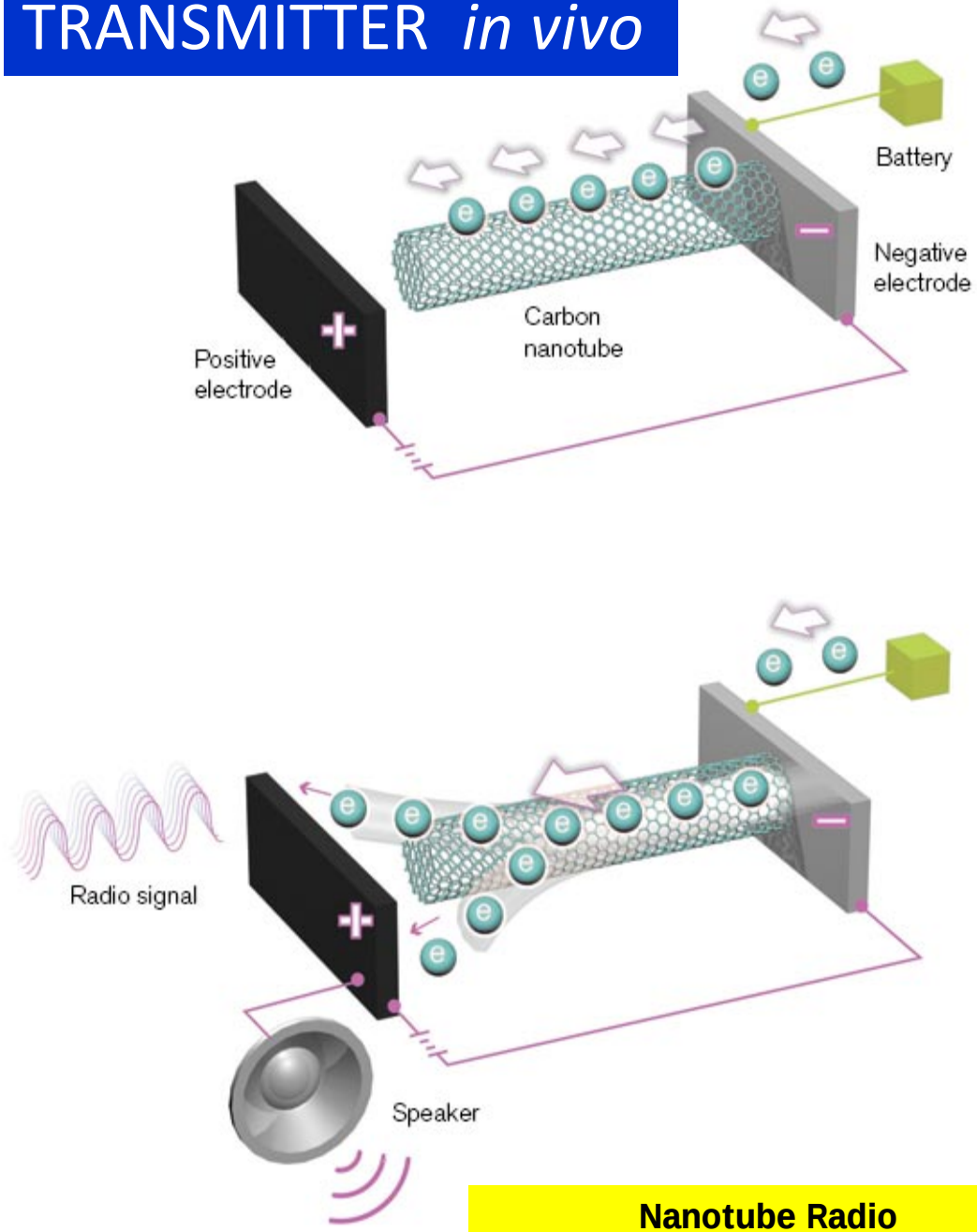
Convergence

MALARIA SENSOR DATA



Blood Glucose Nano-sensor

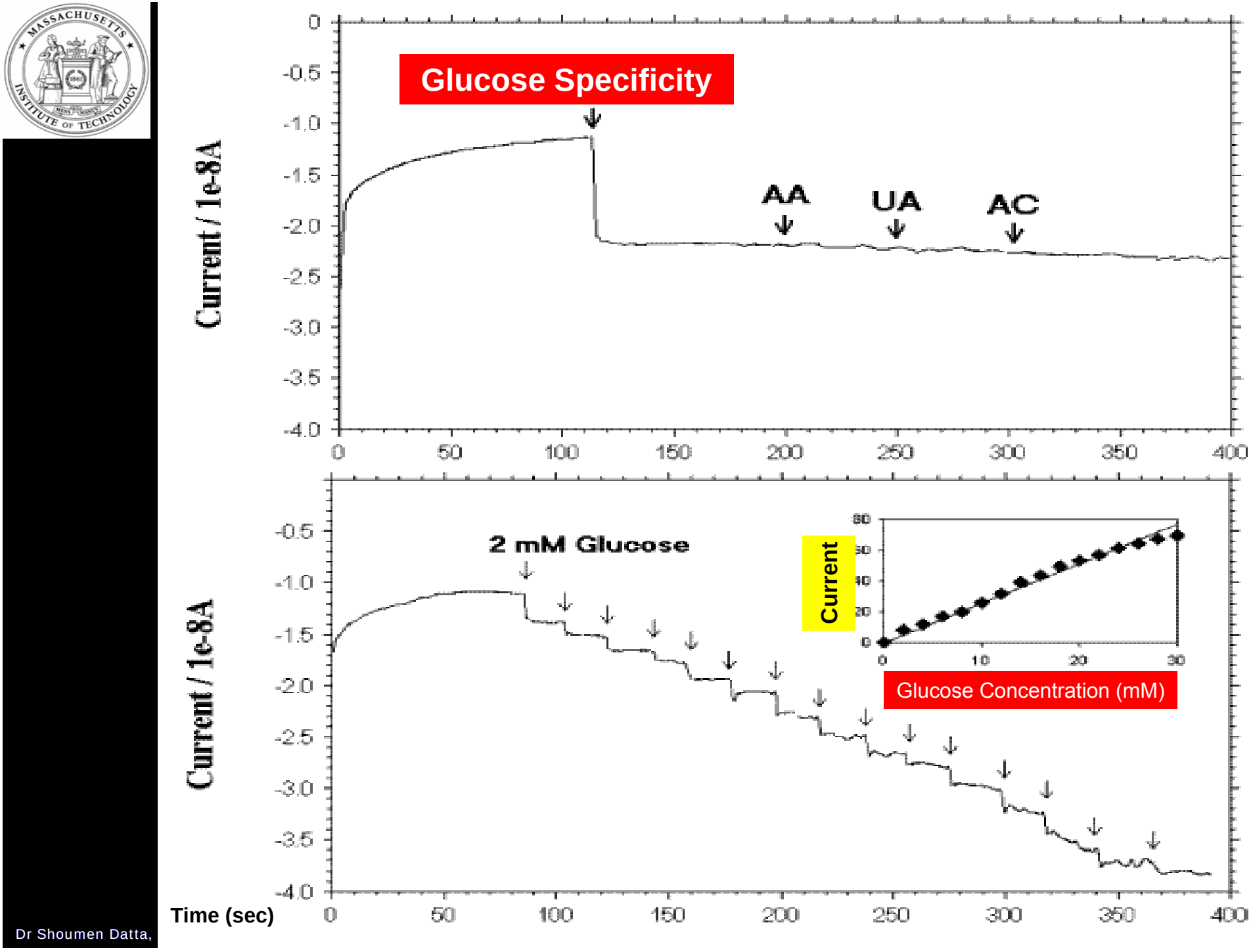
TRANSMITTER *in vivo*



Nanotube Radio

Dr Shoumen Datta, MIT <shoumen@mit.edu>

NanoLetters (2007) 7 3508 – 3511
MIT Tech Review March/April 2008

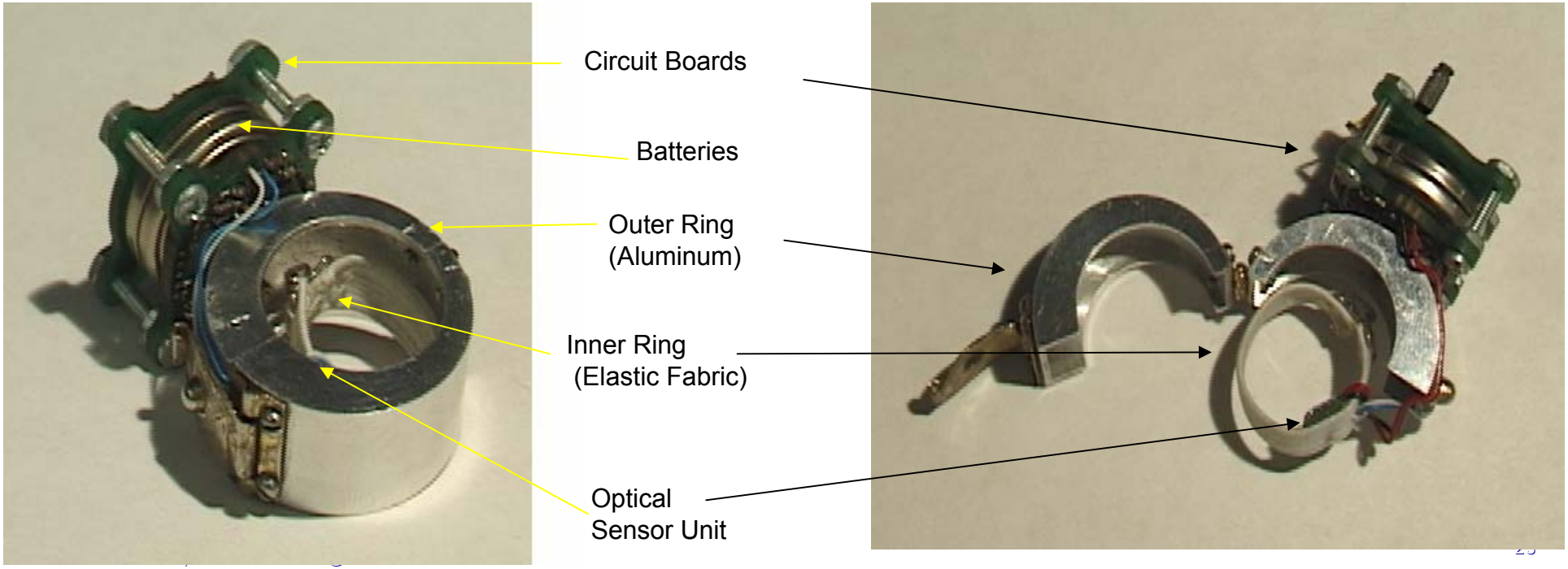

Glucose Specificity
AA
UA
AC
Current / 1e-8A
0
-0.5
-1.0
-1.5
-2.0
-2.5
-3.0
-3.5
-4.0
0
50
100
150
200
250
300
350
400
2 mM Glucose
Current
Glucose Concentration (mM)
Time (sec)

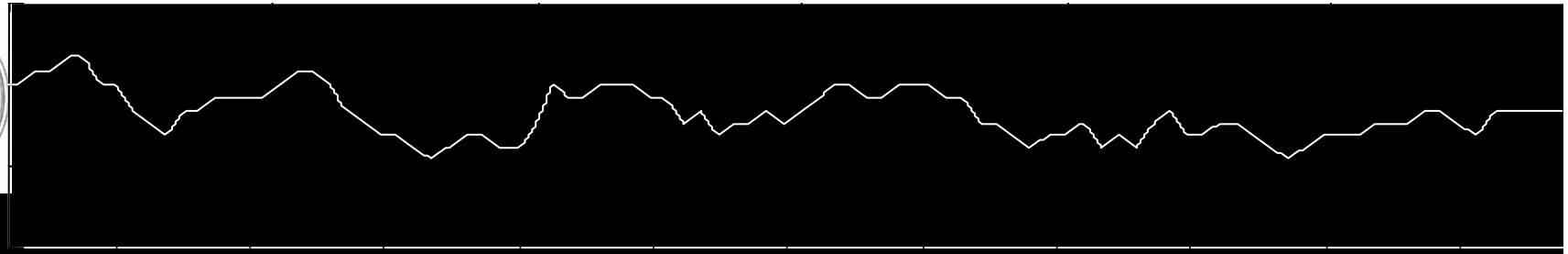
Sensors: Not necessarily *in vivo*, Not necessarily nano

Ring Sensors

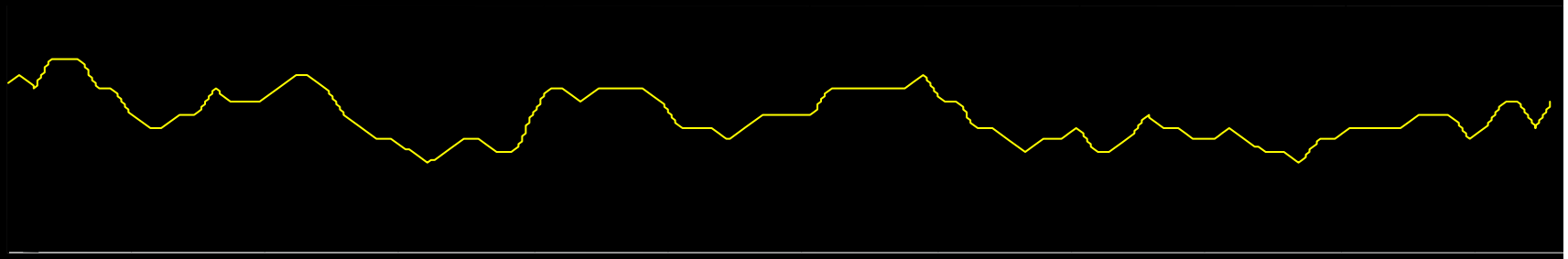
Sokwoo Rhee, Ph.D. thesis, MIT

www.sokwoo.com

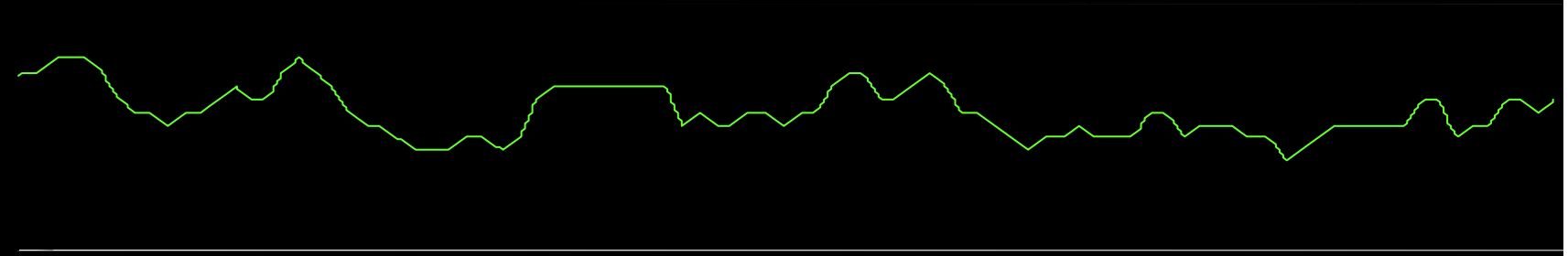




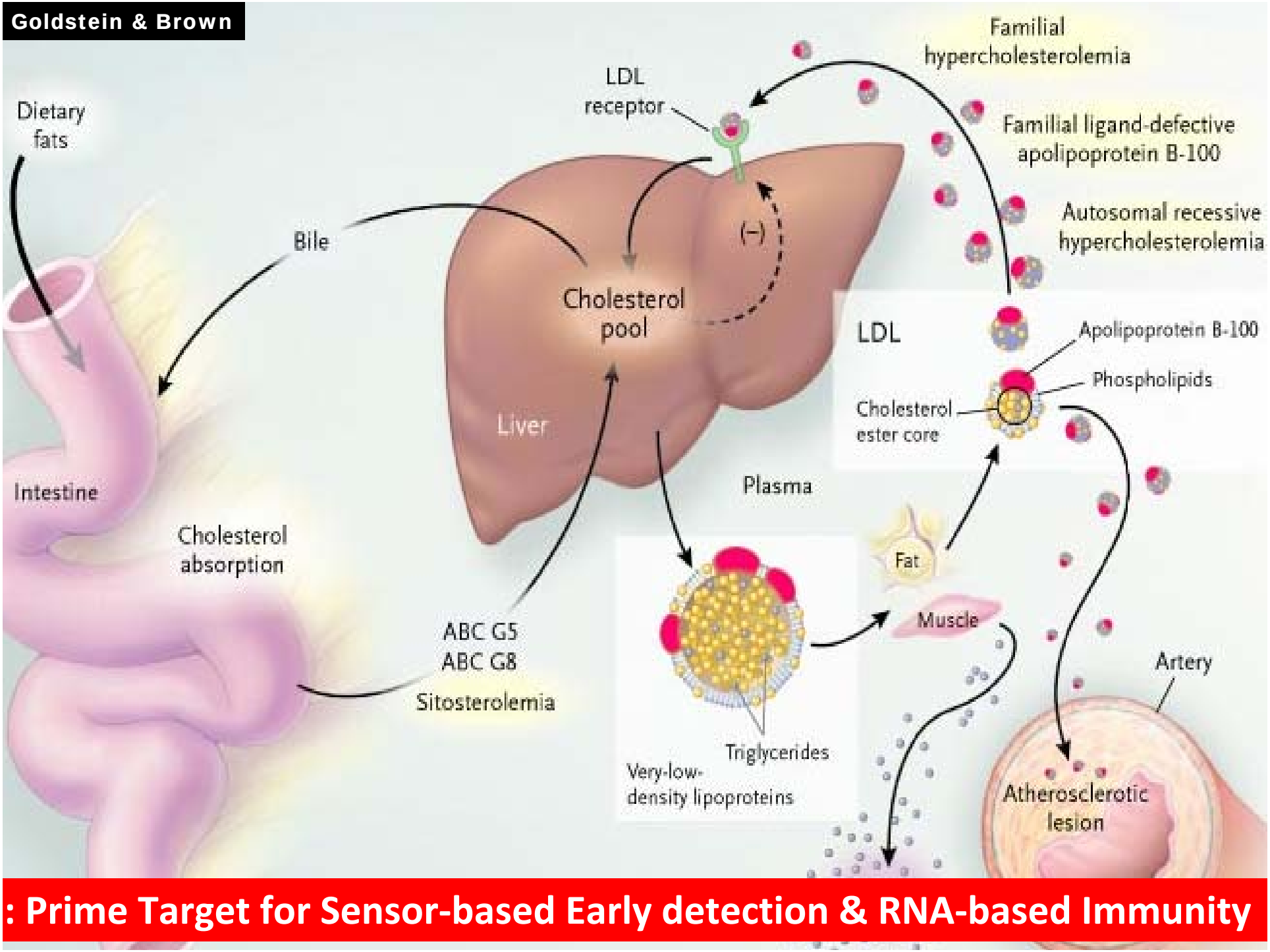
(a) Heart Rate (beats/min) by Electrocardiogram (ECG)



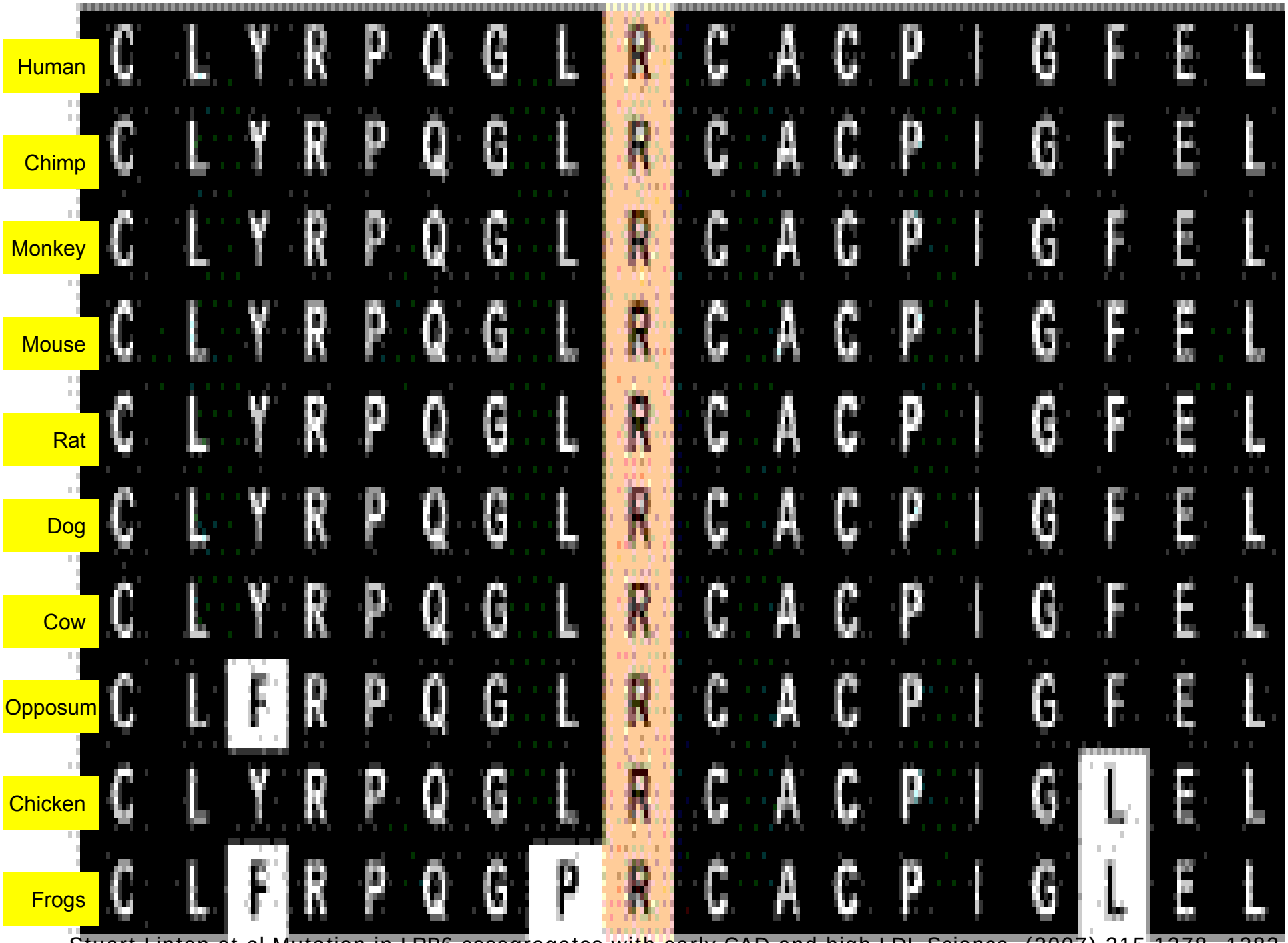
(b) Heart Rate (beats/min) by Fingertip Photoplethymograph (PPG



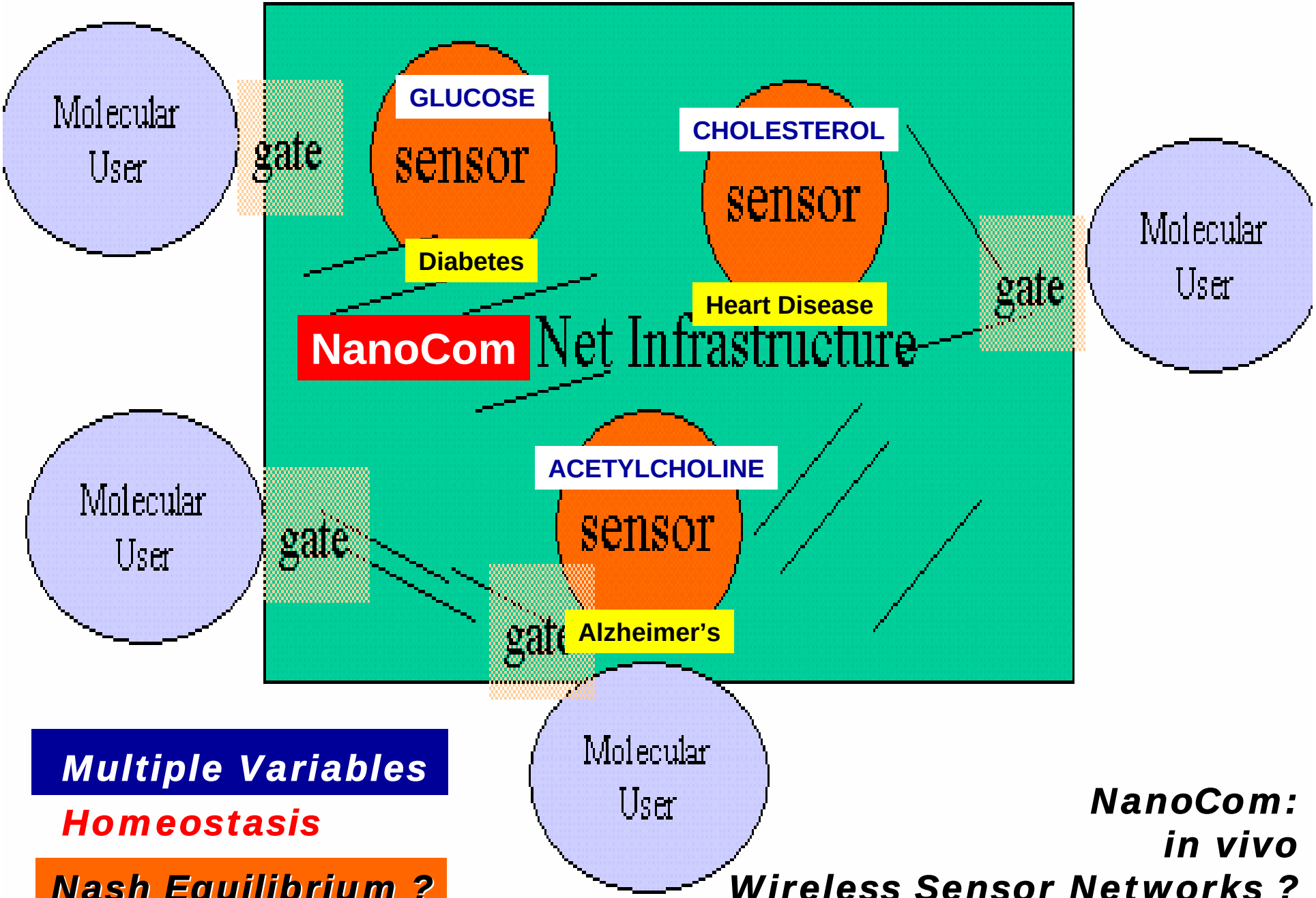
(c) Heart Rate (beats/min) monitored by Wireless Ring Sensor shown in Figure



: Prime Target for Sensor-based Early detection & RNA-based Immunity



Stuart Lipton et al Mutation in LRP6 cosegregates with early CAD and high LDL Science (2007) 315 1278 -1282

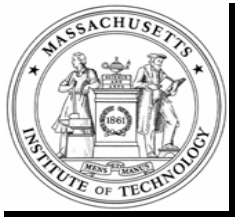


Multiple Variables

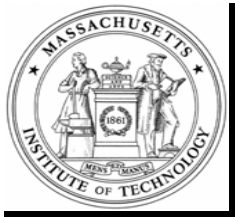
Homeostasis

Nash Equilibrium ?

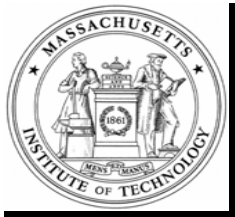
NanoCom: in vivo Wireless Sensor Networks ?



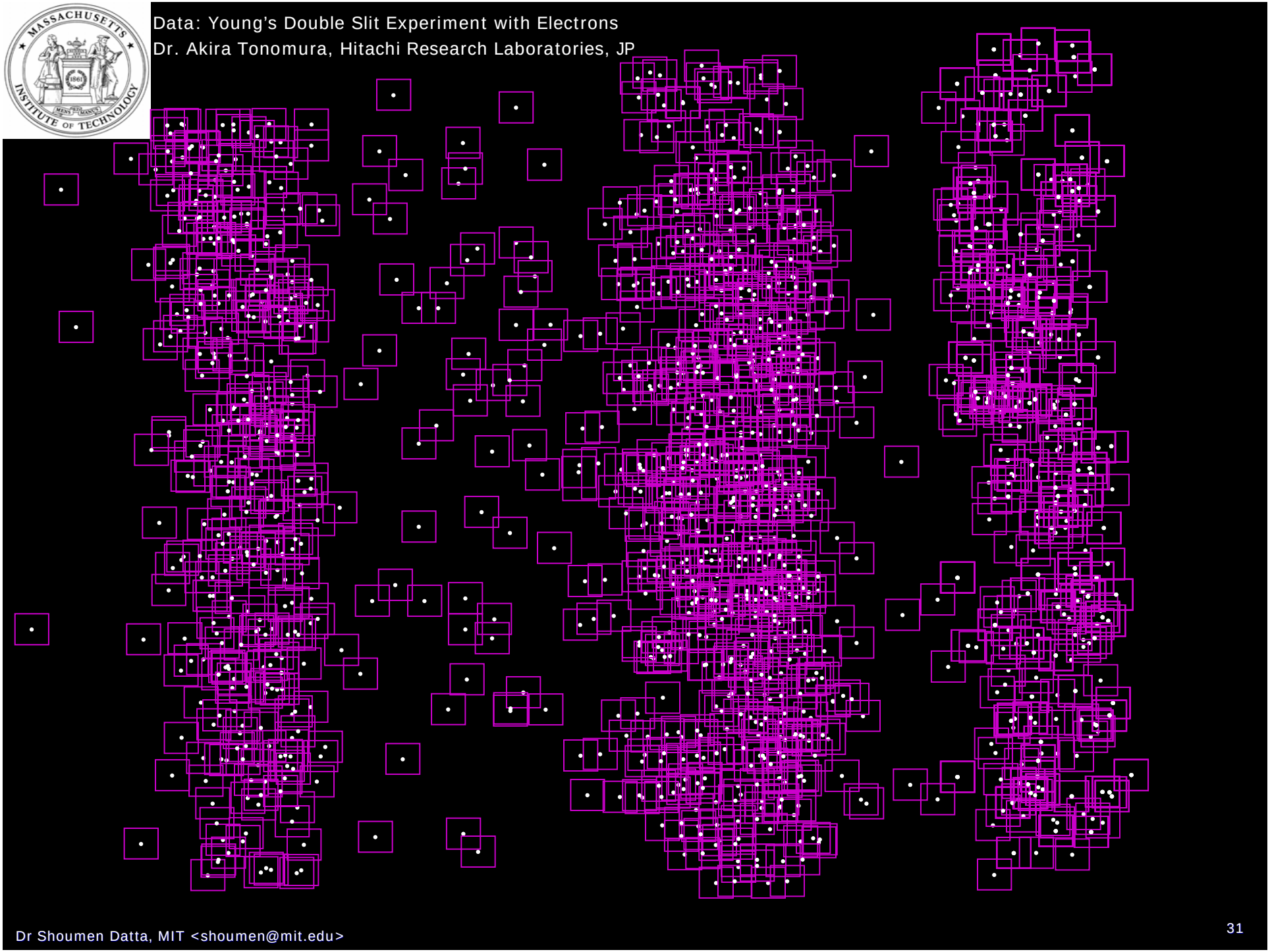
Data…



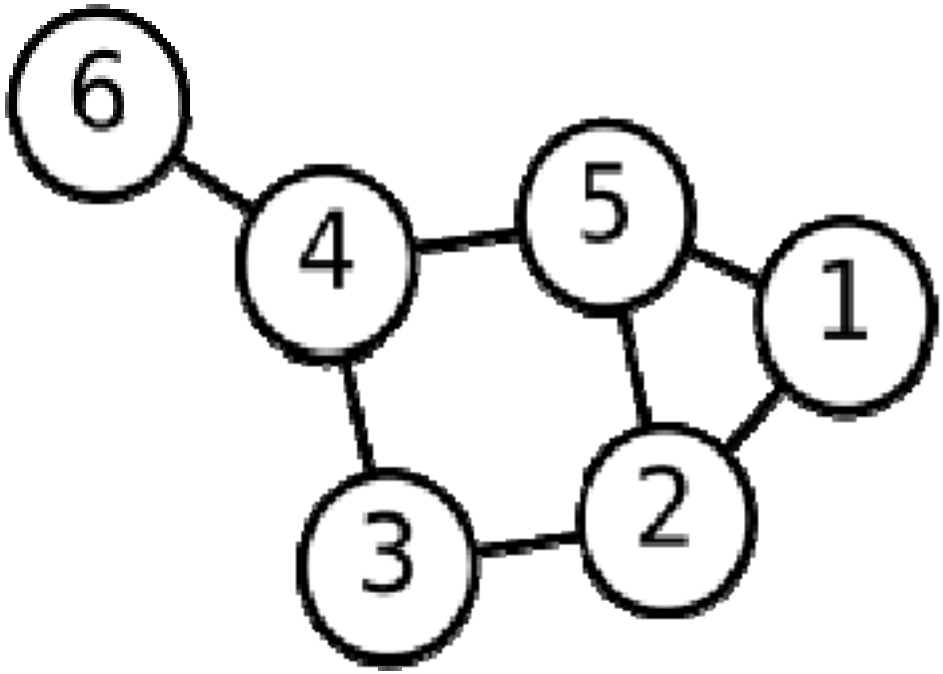
More data points ...

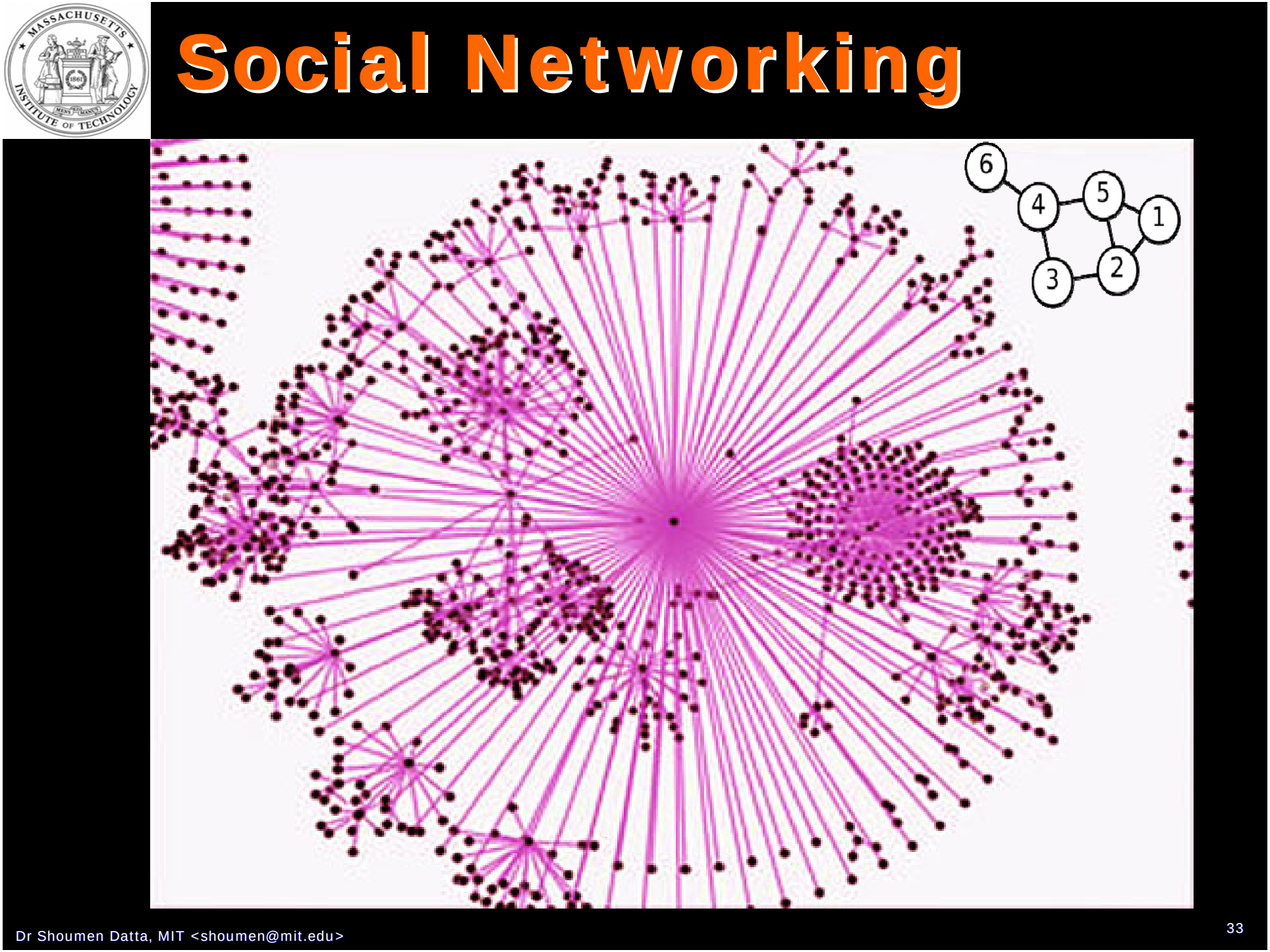


Data shows emerging pattern …

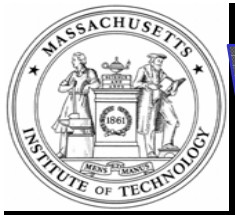

Data: Young's Double Slit Experiment with Electrons
Dr. Akira Tonomura, Hitachi Research Laboratories, JP

Directed Graph: Today's Network





Social Networking



VAR-MGARCH Sense of Distributed Data Analytics

n = 10; p = 1,000
10 locations
1,000 lags

Estimate Coefficients:

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

$$y_{1t} = \beta_0 + \sum_{k=1}^{K} \sum_{i=1}^{N_{x_{kt}}} \alpha_{ki} x_{kt-i} + \varphi_{11} y_{1t-1} + \varphi_{12} y_{2t-1} + \varepsilon_{1t}$$

$$y_{2t} = \beta_0 + \sum_{k=1}^{K} \sum_{i=1}^{N_{x_{kt}}} \alpha_{ki} x_{kt-i} + \varphi_{21} y_{1t-1} + \varphi_{22} y_{2t-1} + \varepsilon_{2t}$$

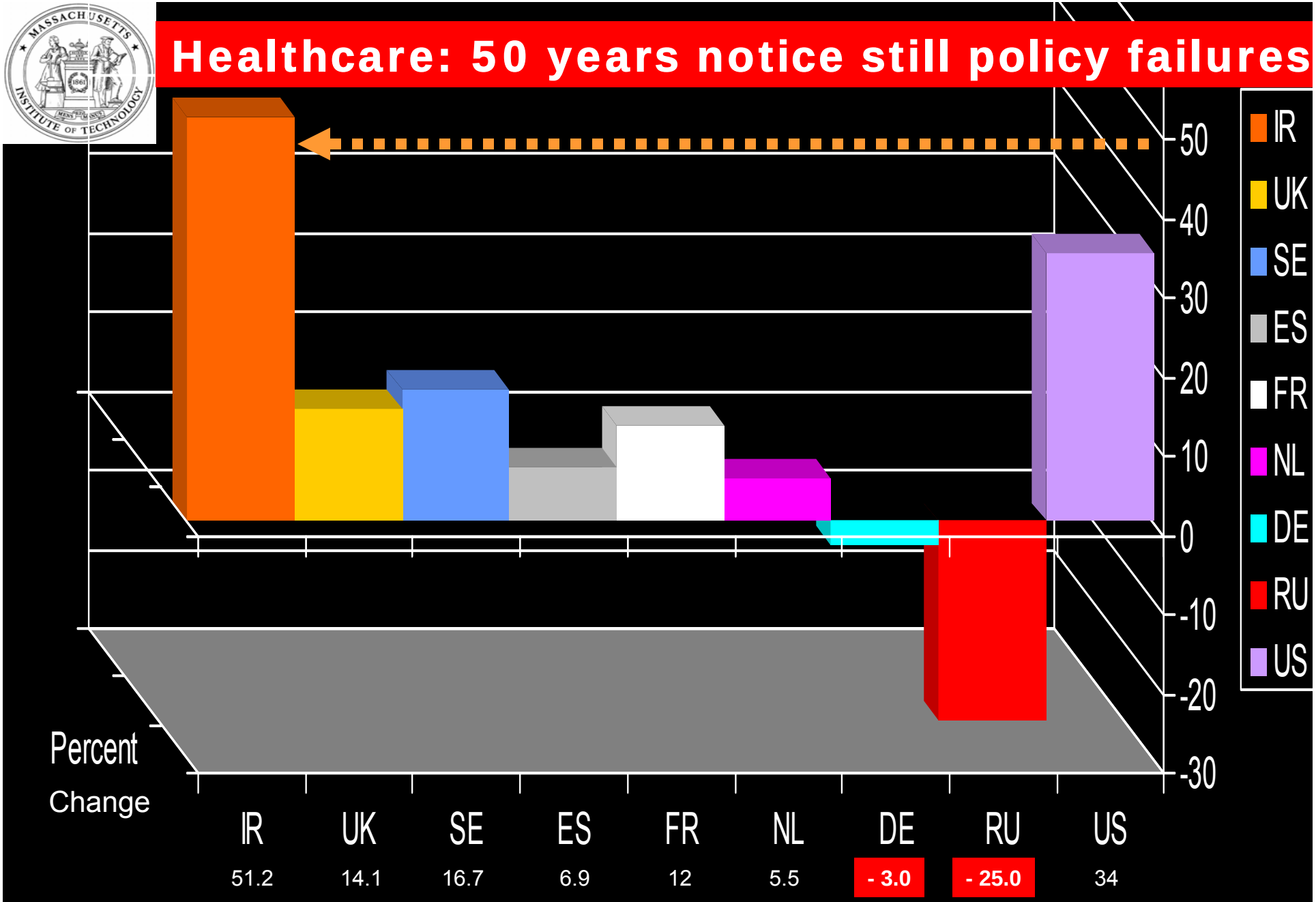
$$\sigma_{1t}^2 = \theta_0 + \sum_{i=1}^{q} \theta_i \varepsilon^2_{1t-i} + \sum_{j=1}^{p} \tau_j \sigma^2_{1t-j}$$

$$\sigma_{2t}^2 = \theta_0 + \sum_{i=1}^{q} \theta_i \varepsilon^2_{2t-i} + \sum_{j=1}^{p} \tau_j \sigma^2_{2t-j}$$

Dr Shoumen Datta, MIT <shoumen@mit.edu>

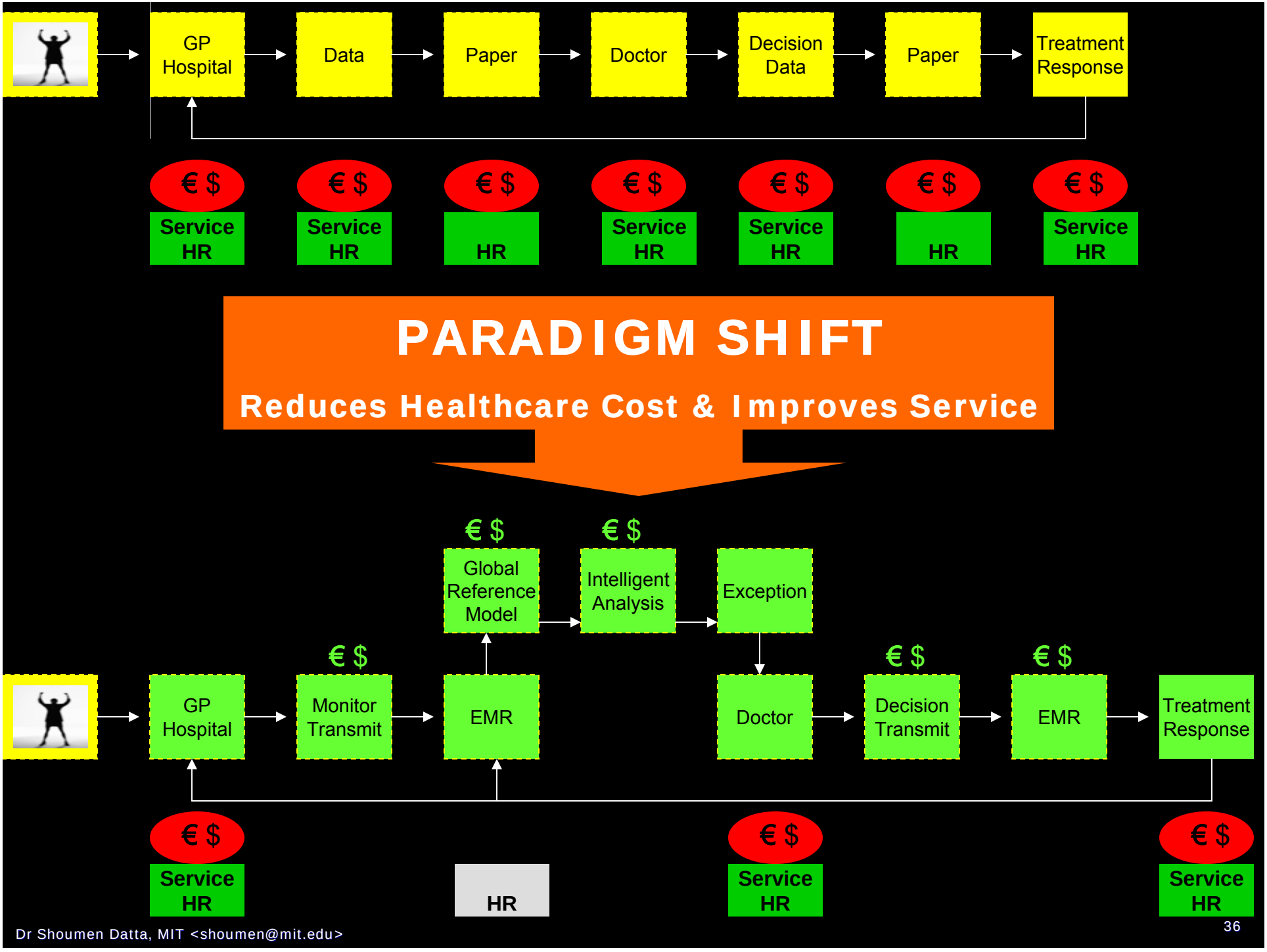
Datta & Granger, 2007

Healthcare: 50 years notice still policy failures

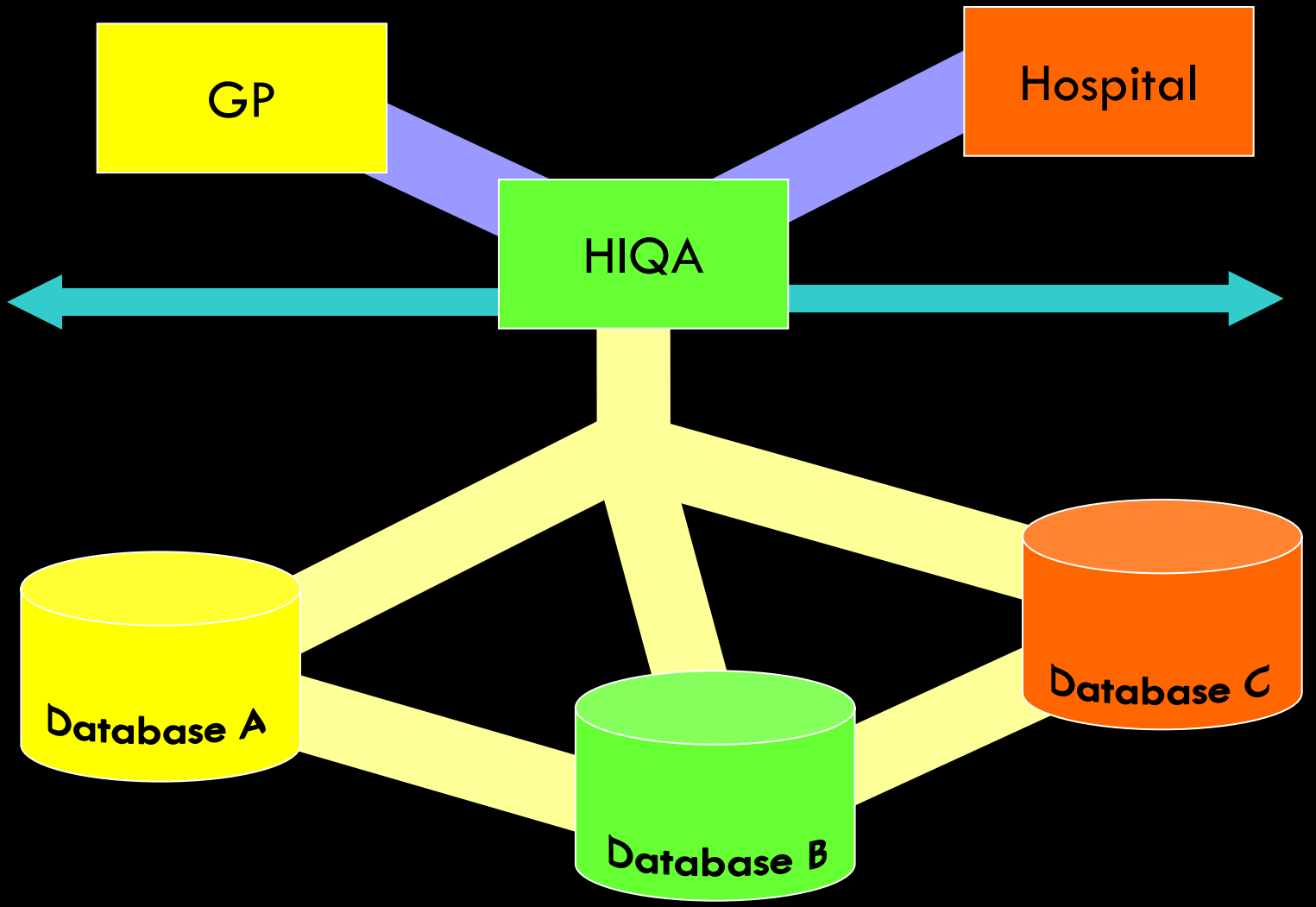


www.populationeurope.org

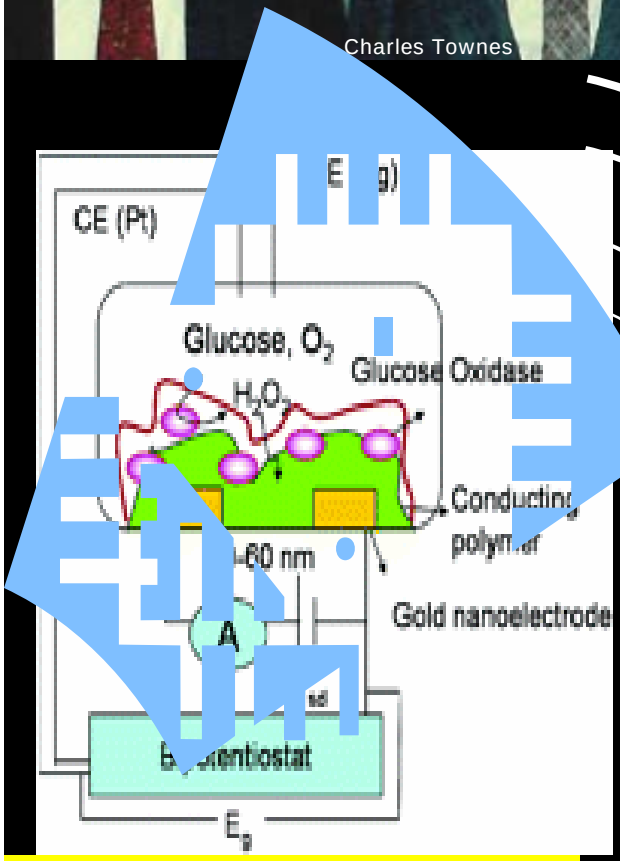
Dr Shoumen Datta, MIT <shoumen@mit.edu>


GP Hospital
Data
Paper
Doctor
Decision Data
Paper
Treatment Response
€ $
Service HR
HR
PARADIGM SHIFT
Reduces Healthcare Cost & Improves Service
Global Reference Model
Intelligent Analysis
Exception
Monitor Transmit
EMR
Doctor
Decision Transmit
EMR
Treatment Response

Data & Information Asymmetry: Isolated DDT Systems



HEALTHCARE MANAGEMENT



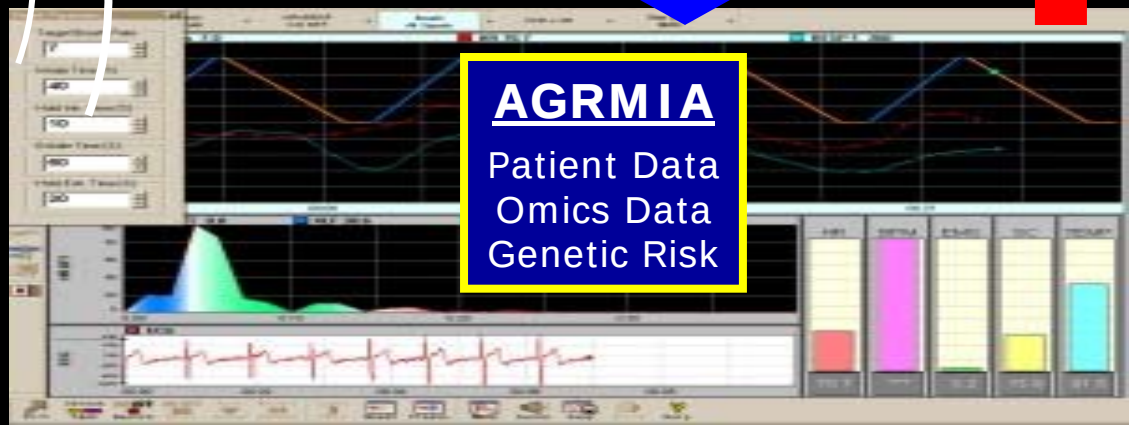
Glucose Nano-sensor Radio

802.11b
WiFi
802.11g

802.16a
Grid

MGH
IDA

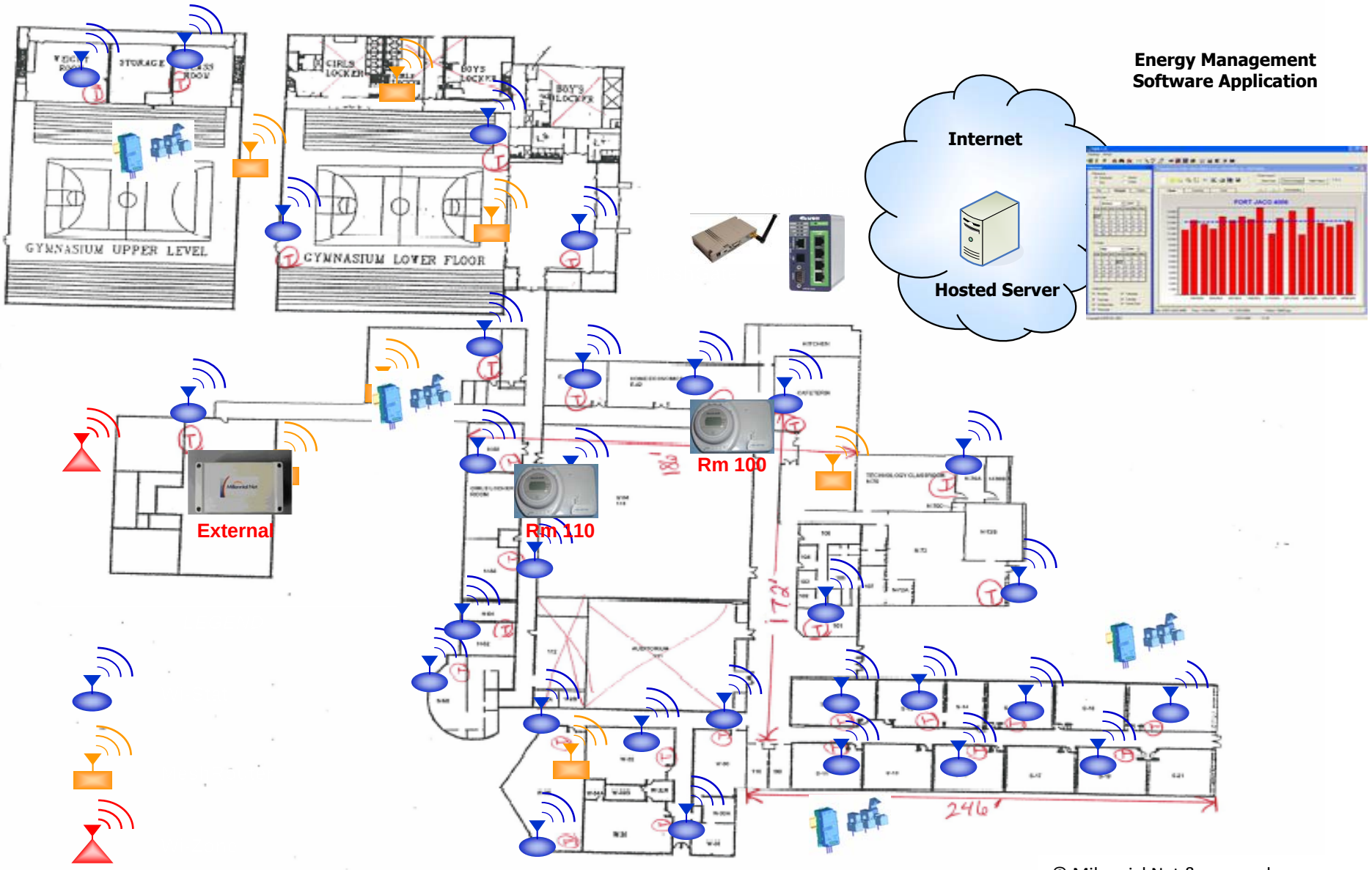
VISIT CLINIC



AGRMIA

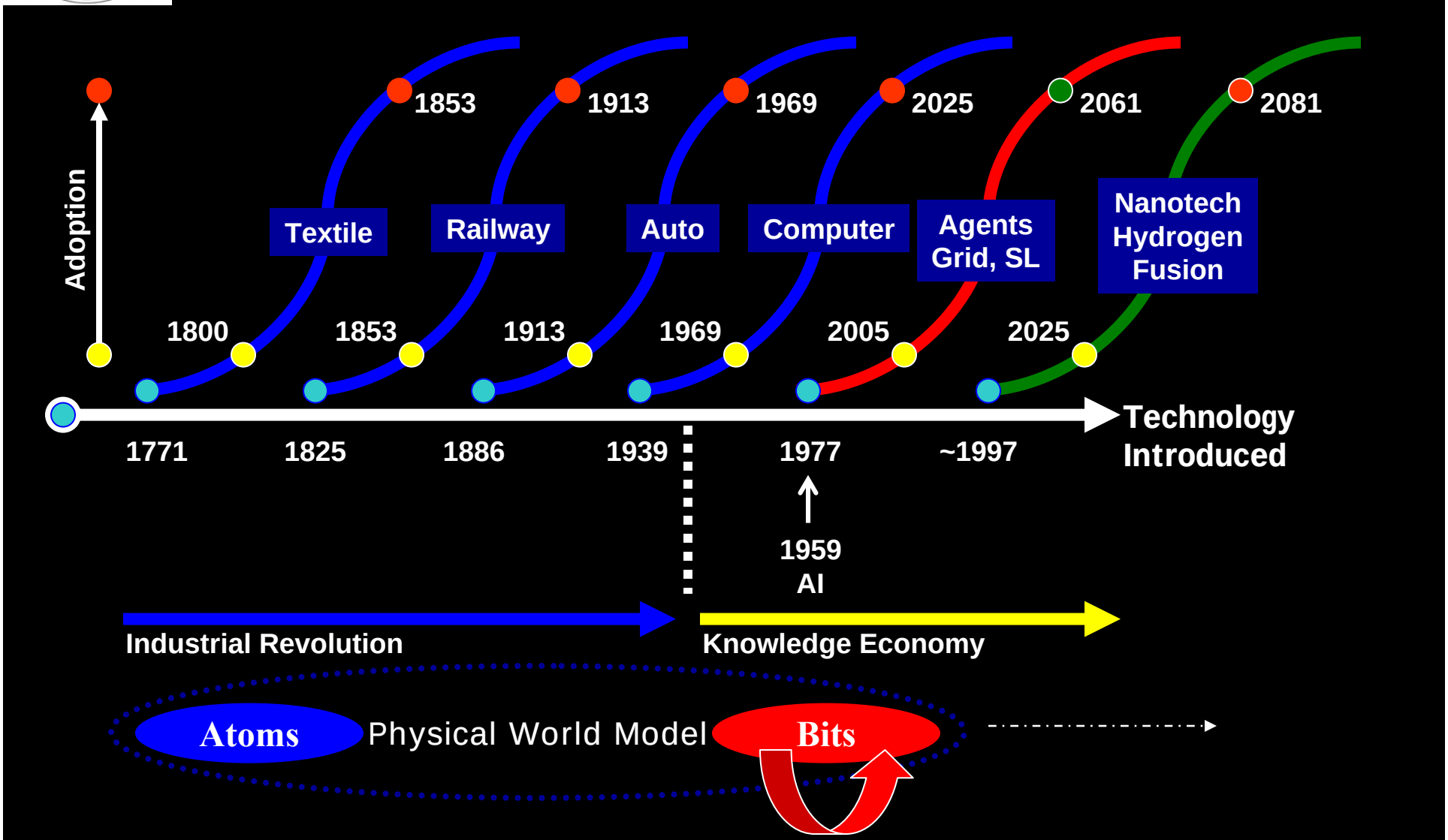
Patient Data
Omics Data
Genetic Risk

ENERGY MANAGEMENT



Dr Shoumen Datta, MIT <shoumen@mit.edu>

Conceptual Convergence and the Wealth of Nations



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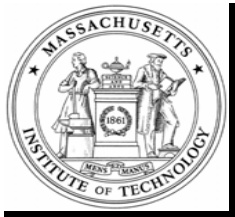

"Did not entail being right all the time. It was rather to dare, to propose new ideas, and then to verify them and to know how to admit errors."

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)