Fractional Order Models of Infectious Diseases

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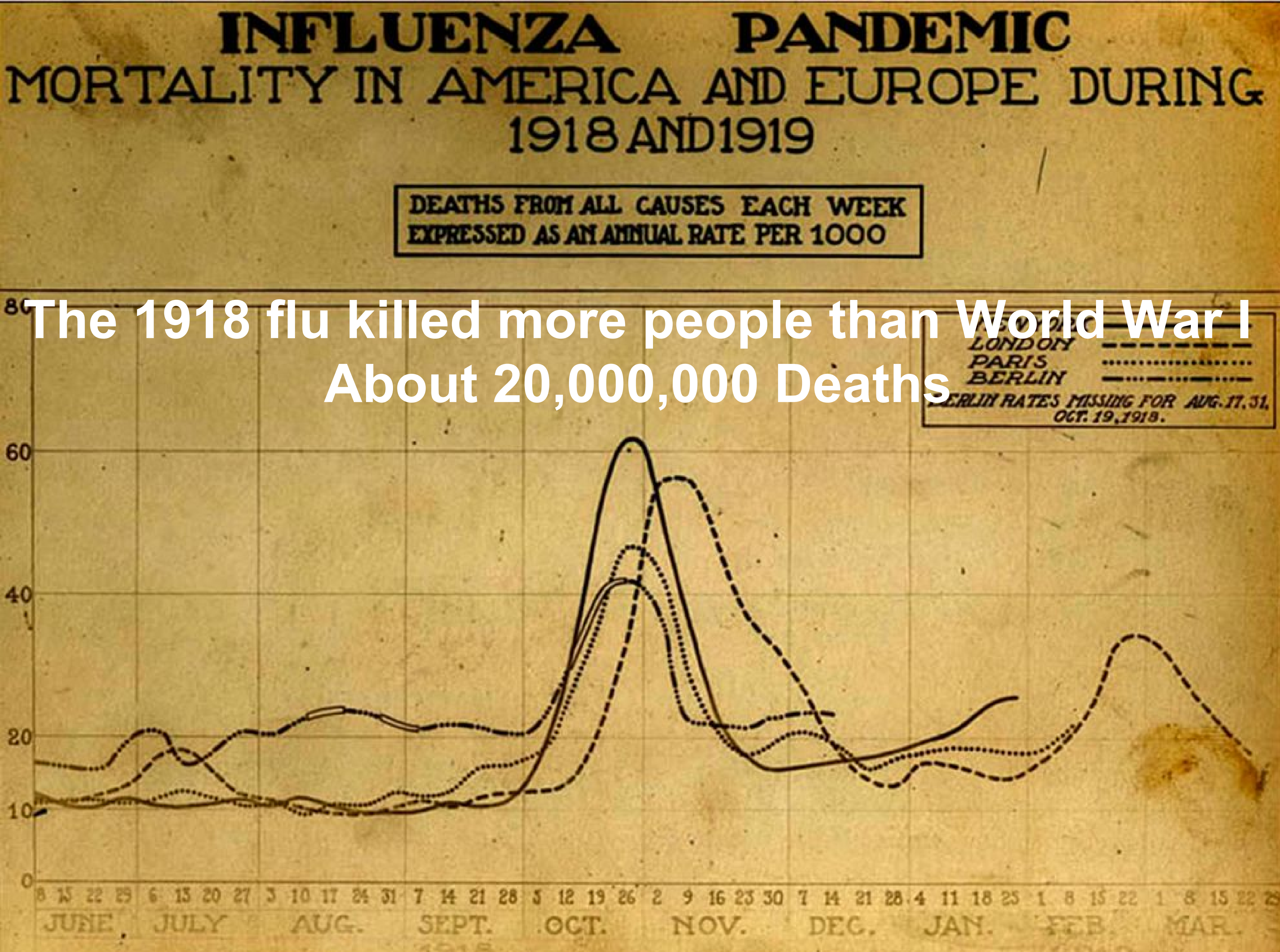
Introduction

Infectious Diseases
Past, Present, and Future

The 1918 flu killed more people than World War I
About 20,000,000 Deaths



The Situation in 2015-2017

- 5.9 million children under age of five died in 2015, i.e. 16 000 every day.
- There are Over 37 million.people infected with HIV.
- 1 million people died from AIDS in 2015.
- The recent outbreaks of Ebola have led to 11000 of deaths in 2015.

Economic Impact of infectious Diseases is terrible

West Africa suffered up to $32 billion loss during Ebola outbreak.

What mathematical models can do to help?

- To know How large Will the Outbreak be and how fast the epidemic transmits.

- To assist the decision makers to put their strategies to control the diseases.

- To understand the dynamics and transmission of diseases to activate the vaccination programs and to test Vaccine efficacy in blocking disease transmission.

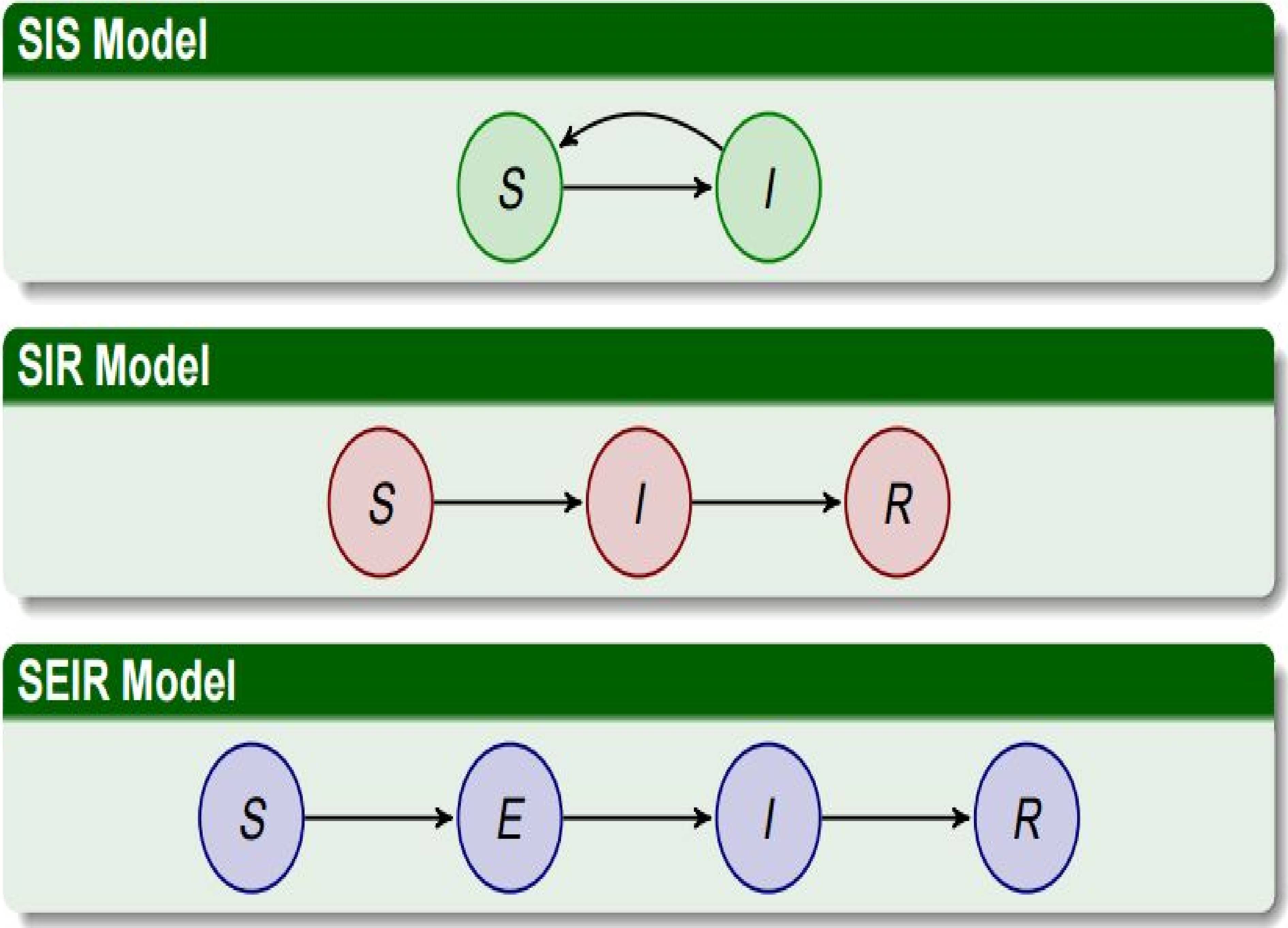
Before Differential Equations Models:
Bernoulli Model

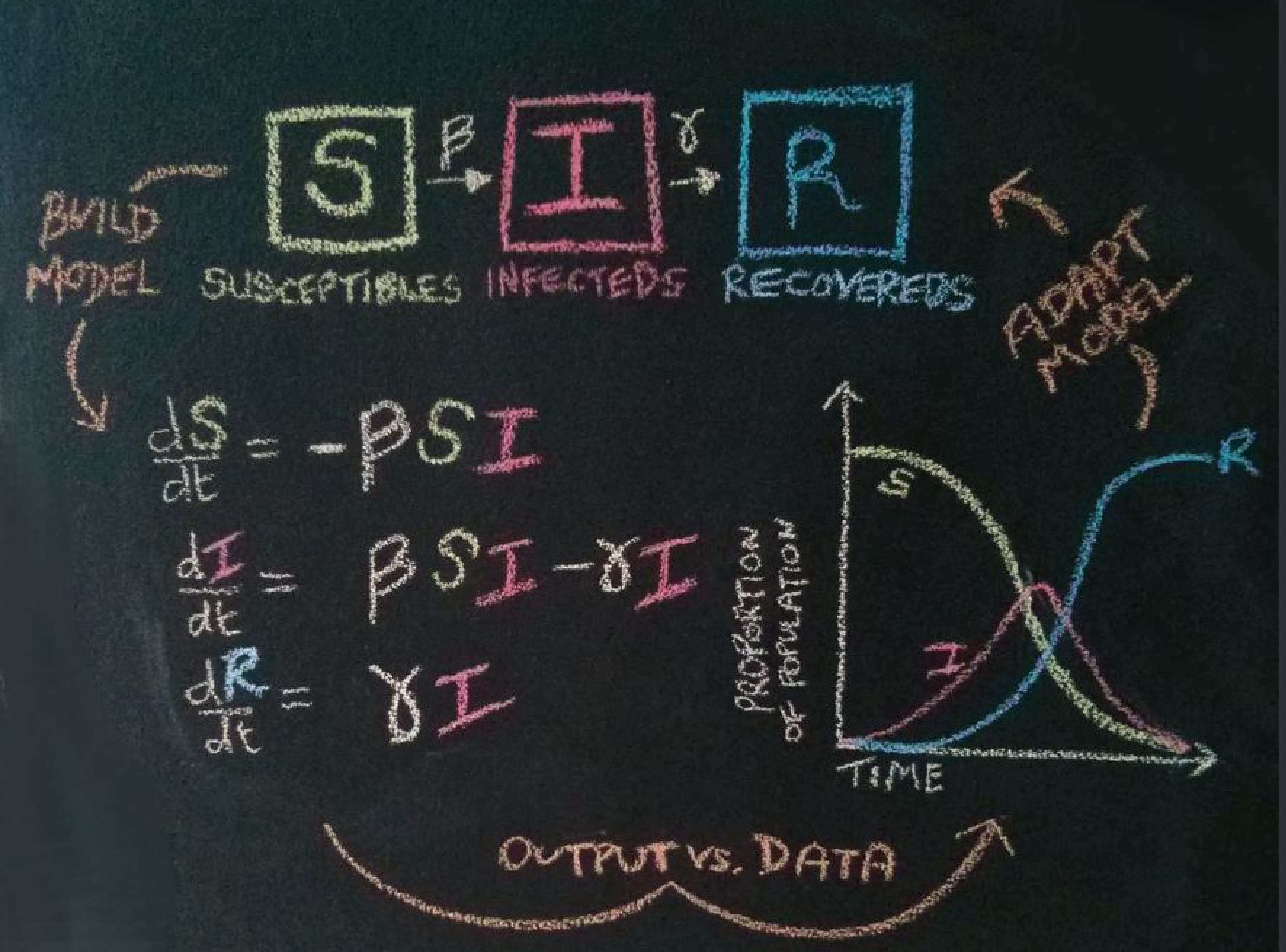
"I simply wish that, in a matter which so closely concerns the well-being of mankind, no decision shall be made without all the knowledge which a little analysis and calculation can provide."

Daniel Bernoulli,

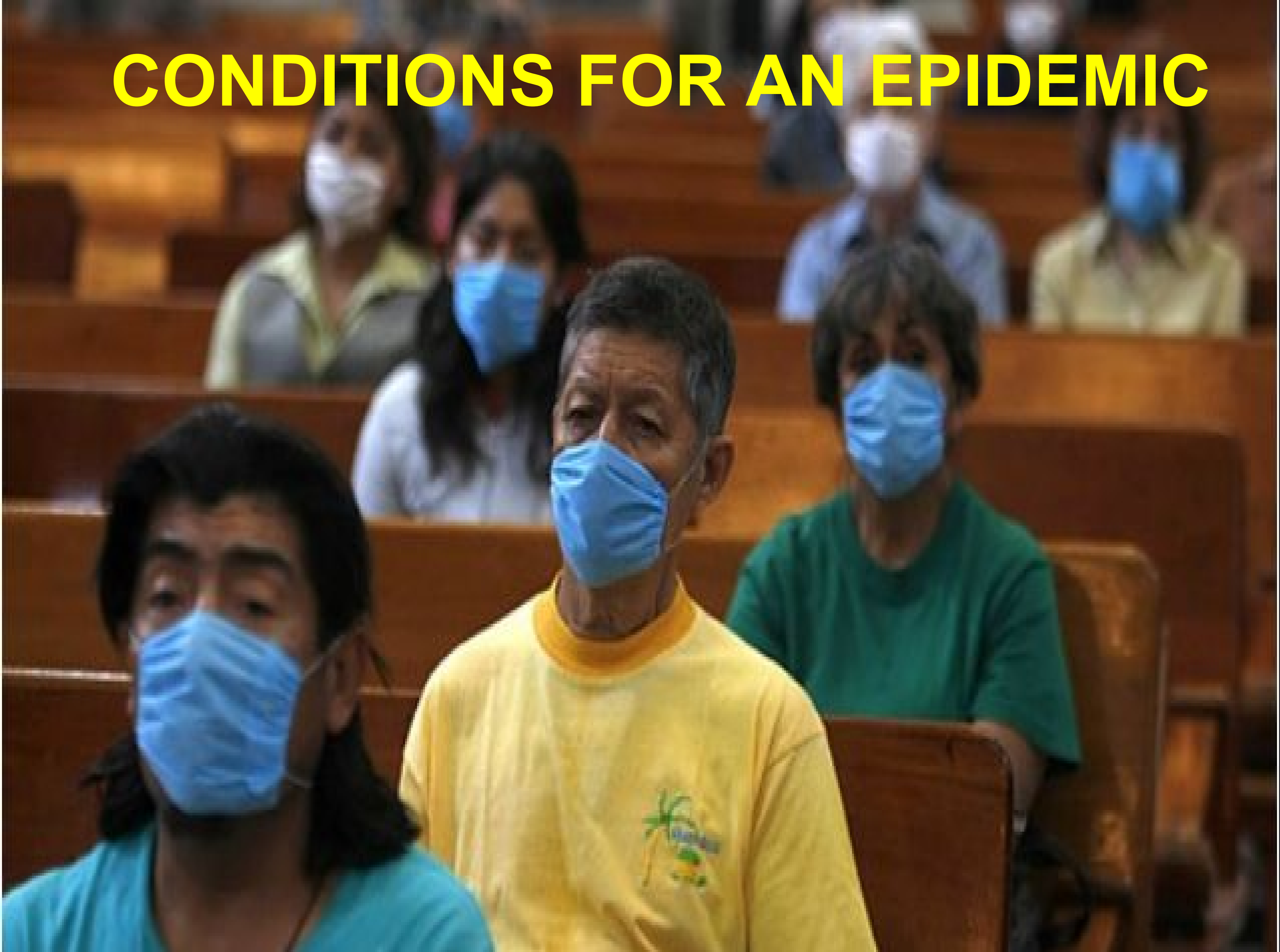
Daniel Bernoulli
1700-1782

Differential Equations Models of infectious diseases


SIS Model
S
I
SIR Model
S
I
R
SEIR Model
S
E
I
R


S
β
I
γ
R
BUILD MODEL
SUSCEPTIBLES
INFECTEDS
RECOVEREDS
ADAPT MODEL
dS/dt = -βSI
dI/dt = βSI - γI
dR/dt = γI
PROPORTION OF POPULATION
TIME
S
I
R
OUTPUT VS. DATA

CONDITIONS FOR AN EPIDEMIC



THE BASIC REPRODUCTION NUMBER "R_0"

" R_0 " is The mean number of secondary infections generated by a single infected in a completely susceptible population

Conditions for an Epidemic

- If $R_0 > 1$ an epidemic occurs in the absence of intervention.
- If $R_0 < 1$ the disease dies out.

R_0 for the Basic SIR Model$= \frac{\beta}{\gamma}$

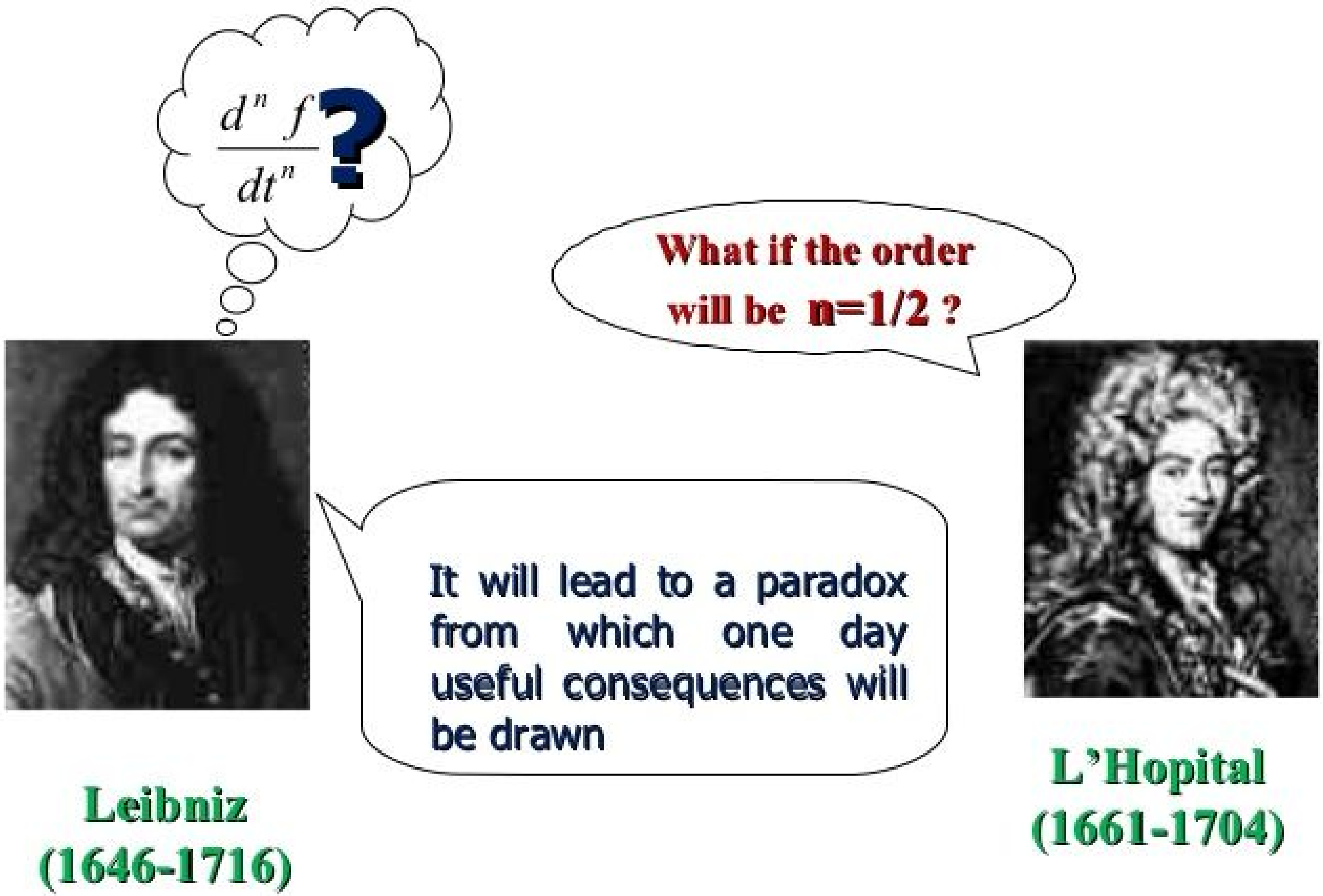
But these classical integer models carry no info about memory of Host or vector.

mathematical models with memory

- Delay differential equations
- Fractional differential equations

Fractional Calculus
Brief Summary

History of fractional calculus



Let $f : [a, b] \to \mathbb{R}$ be a function, α a positive real number, n the integer satisfying $n-1 \leq \alpha < n$, and Γ the Euler gamma function. Then,

1. the left and right Riemann–Liouville fractional integrals of order α are defined by

$$ {}_aI_x^\alpha f(x) = \frac{1}{\Gamma(\alpha)} \int_a^x (x-t)^{\alpha-1} f(t)dt, $$

   and

$$ {}_xI_b^\alpha f(x) = \frac{1}{\Gamma(\alpha)} \int_x^b (t-x)^{\alpha-1} f(t)dt, $$

   respectively;

2. the left and right Riemann–Liouville fractional derivatives of order α are defined by

$$ {}_aD_x^\alpha f(x) = \frac{d^n}{dx^n} {}_aI_x^{n-\alpha} f(x) = \frac{1}{\Gamma(n-\alpha)} \frac{d^n}{dx^n} \int_a^x (x-t)^{n-\alpha-1} f(t)dt, $$

and

$$ {}_xD_b^\alpha f(x) = (-1)^n \frac{d^n}{dx^n} {}_xI_b^{n-\alpha} f(x) = \frac{(-1)^n}{\Gamma(n-\alpha)} \frac{d^n}{dx^n} \int_x^b (t-x)^{n-\alpha-1} f(t)dt, $$

respectively;

3. the left and right Caputo fractional derivatives of order α are defined by

$$ {}_a^CD_x^\alpha f(x) = {}_aI_x^{n-\alpha} \frac{d^n}{dx^n} f(x) = \frac{1}{\Gamma(n-\alpha)} \int_a^x (x-t)^{n-\alpha-1} f^{(n)}(t)dt, $$

and

$$ {}_x^CD_b^\alpha f(x) = (-1)^n {}_xI_b^{n-\alpha} \frac{d^n}{dx^n} f(x) = \frac{1}{\Gamma(n-\alpha)} \int_x^b (-1)^n (t-x)^{n-\alpha-1} f^{(n)}(t)dt, $$

respectively.

Fractional derivatives have the unique property of capturing the history of the variable, that is, they have memory. This cannot be easily done by means of the integer order derivatives.

WHAT IS THE PHYSICAL MEANING OF THE FRACTIONAL ORDER DERIVATIVE?

The physical meaning of the fractional order is considered to be the index of memory. In the models with memory, a memory process usually consists of two stages:

- Short stage with permanent retention,
- The other is governed by a simple model of fractional derivative.

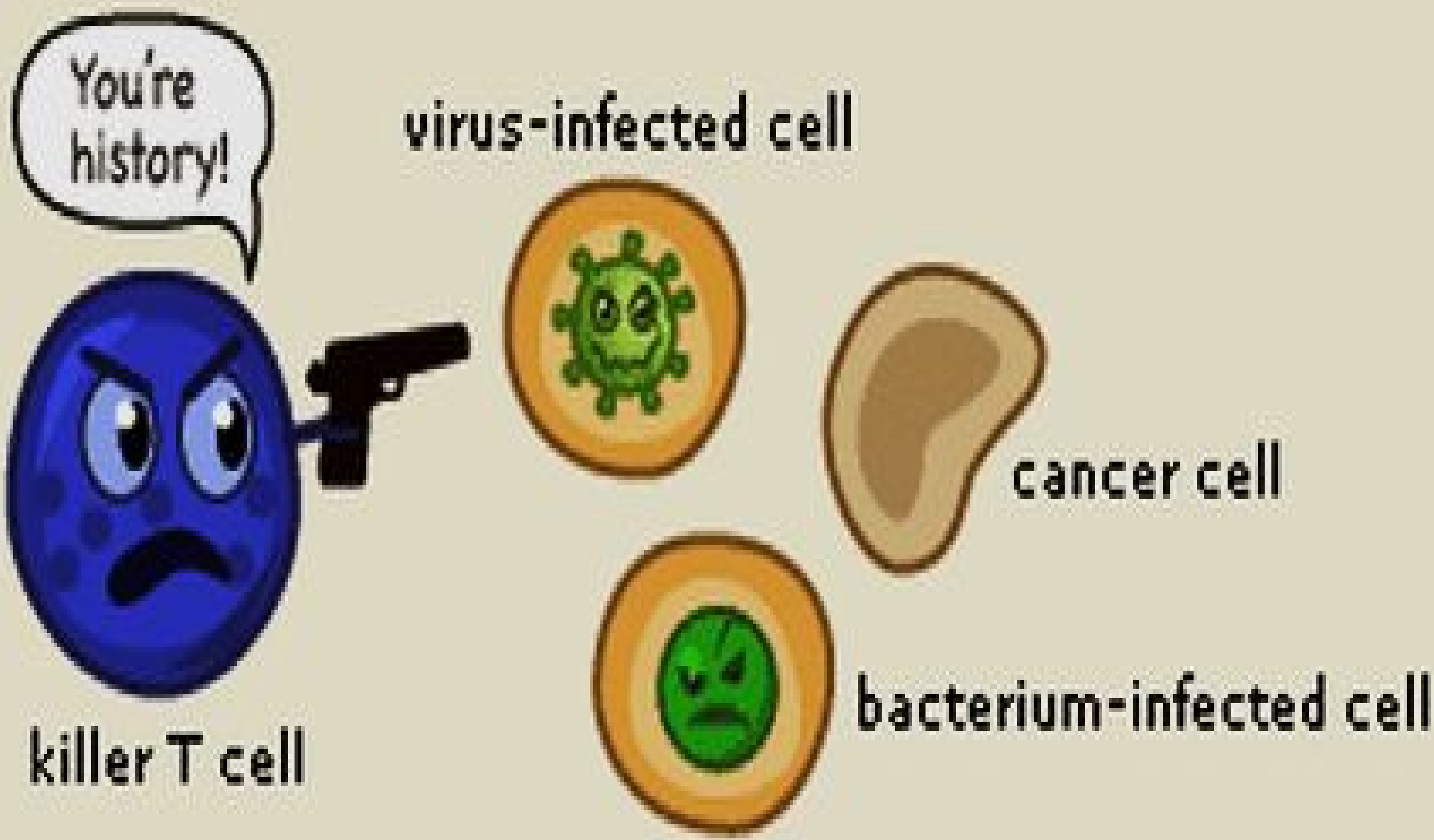
- M. Du, Z. Wang and H. Hu, Measuring memory with the order of fractional derivative. Sci. Rep. 3(2013).
- K. Moaddy, A.G. Radwan, K.N. Salama, S. Momani, I. Hashim, The fractional-order modeling and synchronization of electrically coupled neuron systems, Comput. Math. Appl. 64 (2012) 3329–3339.

Two main advantages of using fractional-order models:

- The system response at any time will be affected by all previous responses.

- Fractional-order parameter enriches the system performance through increasing one degree of freedom which extends the system to more space.

Memory of immune system



The killer T cells terminate cancer cells and cells infected by a virus or bacterium.

IMMUNE SYSTEM MODEL WITH MEMORY

$$D^{\alpha}(x) = x - axy - bxz,$$
$$D^{\alpha}(y) = -cy + xy,$$
$$D^{\alpha}(z) = -ez + xz.$$

y, and z are two immune effectors attacking an antigen x.

where $0 < \alpha \leq 1$ is the index of memory.

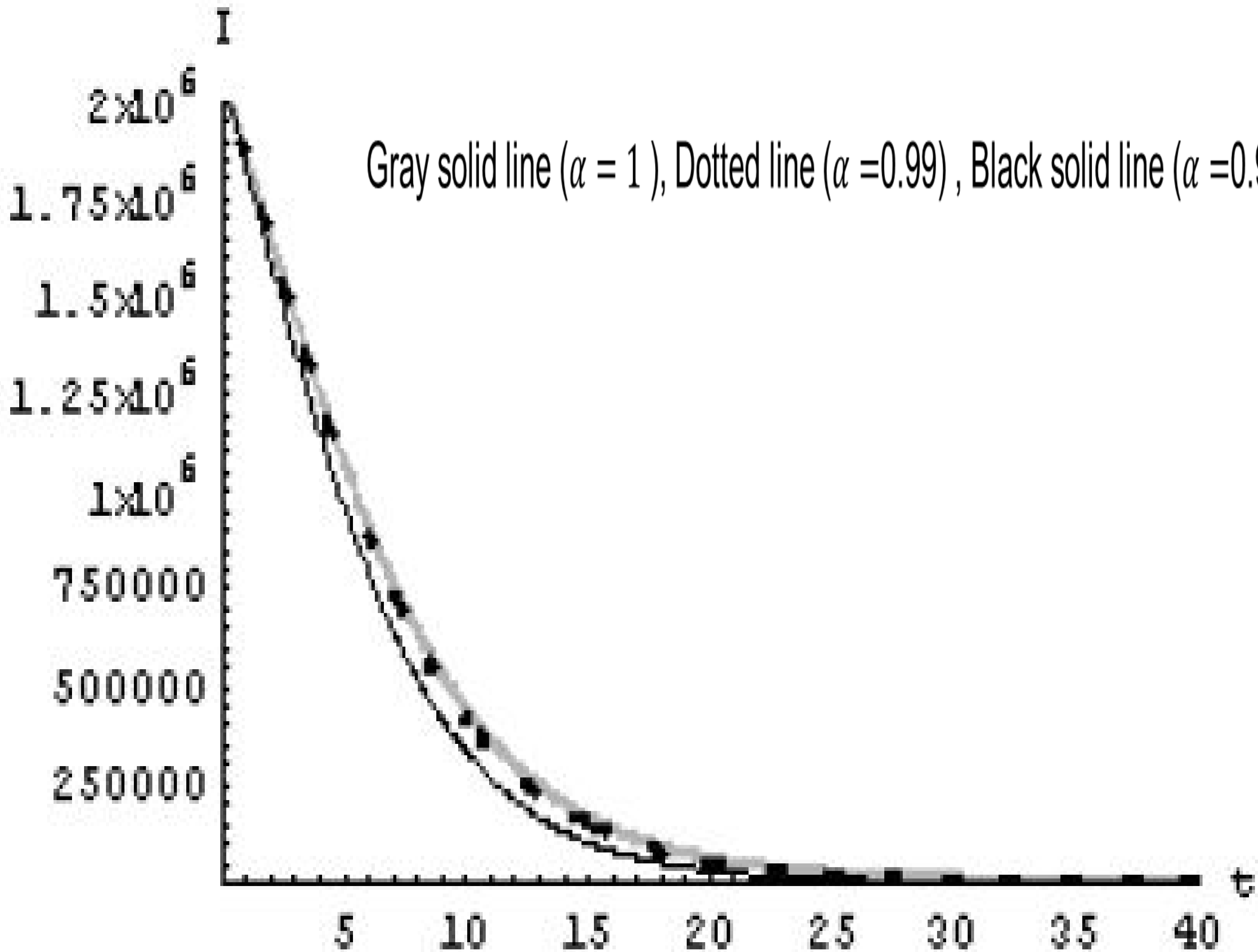
A.H. Hashish, E. Ahmed, Towards understanding the immune system, Theor. Biosci. 126 (2–3) (2007) 61–64.

Fractional order HCV MODEL

$$D^{\alpha}(T) = s - dT - (1-\eta)\beta VT,$$
$$D^{\alpha}(I) = (1-\eta)\beta VT - \delta\, I(1 - I/c_2)\,,$$
$$D^{\alpha}(V) = (1-\varepsilon_p)pI - cV.$$

T represents uninfected hepatocytes,
I represents infected hepatocytes,
V represents virus Density,
and $0 < \alpha \leq 1$ is the index of memory.

E. Ahmed and H.A. El-Saka, On fractional order models for Hepatitis C, Nonlinear Biomed. Phys. 4 (2010).



I
2×10^6
1.75×10^6
1.5×10^6
1.25×10^6
1×10^6
750000
500000
250000
Gray solid line (α = 1), Dotted line (α =0.99) , Black solid line (α =0.95).
5
10
15
20
25
30
35
40
t

Arafa *et al. Nonlinear Biomedical Physics* 2012, **6**:1
http://www.nonlinearbiomedphys.com/content/6/1/1

NONLINEAR BIOMEDICAL PHYSICS

RESEARCH **Open Access**

Fractional modeling dynamics of HIV and CD4$^+$ T-cells during primary infection

AAM Arafa[1*], SZ Rida[1] and M Khalil[2]

Abstract

In this paper, we introduce fractional-order into a model of HIV-1 infection of CD4$^+$ T cells. We study the effect of the changing the average number of viral particles *N* with different sets of initial conditions on the dynamics of the presented model. Generalized Euler method (GEM) will be used to find a numerical solution of the HIV-1 infection fractional order model.

$$D^{\alpha_1}(T) = s - KVT - dT + bI,$$
$$D^{\alpha_2}(I) = KVT - (b + \delta)I,$$
$$D^{\alpha_3}(V) = N\delta I - cV.$$

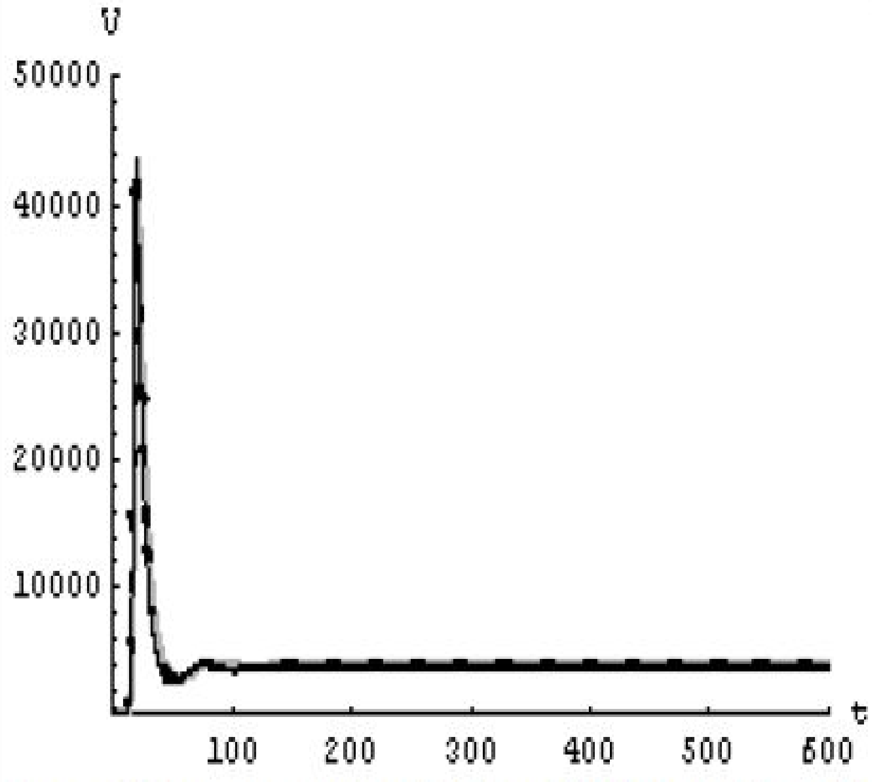


Figure 9 The concentration of the free HIV virus particles at N = 1600 in the 1st case. Gray solid line (α = 1), Dotted line (α = 0.99), Black solid line (α = 0.95).

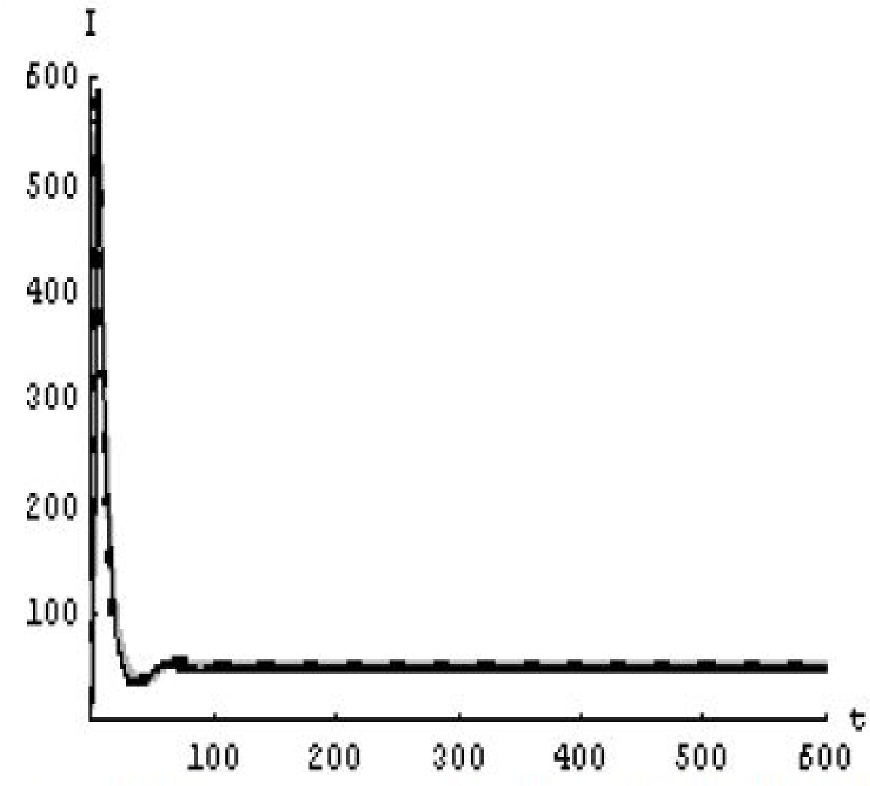


Figure 11 The concentration of the infected $CD4^+$ T cells at N = 1600 in the 2nd case. Gray solid line (α = 1), Dotted line (α = 0.99), Black solid line (α = 0.95).

International Journal of Biomathematics
Vol. 7, No. 4 (2014) 1450036 (11 pages)

DOI: 10.1142/S1793524514500363

World Scientific
www.worldscientific.com

A fractional-order model of HIV infection: Numerical solution and comparisons with data of patients

$$D^{\alpha_1}(T) = s - dT - kVT,$$

$$D^{\alpha_2}(T^*) = kVT - (\delta + d_x E)T^*,$$

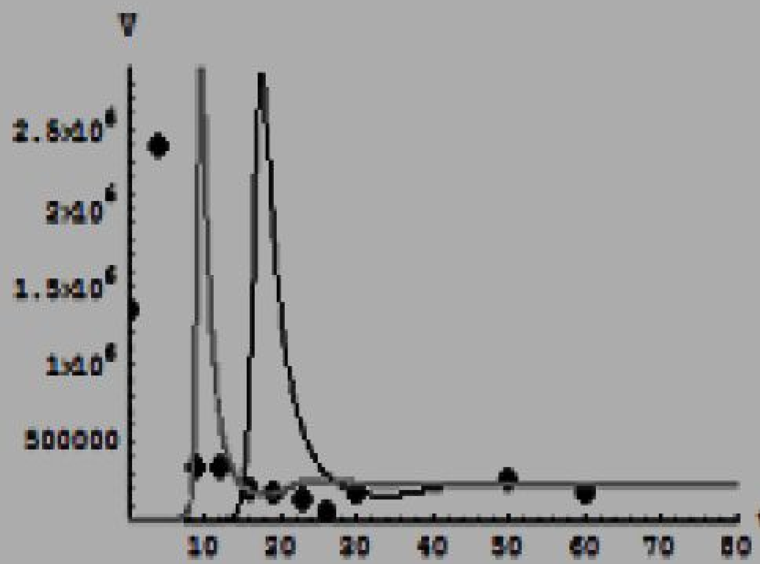
$$D^{\alpha_3}(V) = N\delta T^* - cV,$$

$$D^{\alpha_4}(E) = pT^* - d_E E,$$

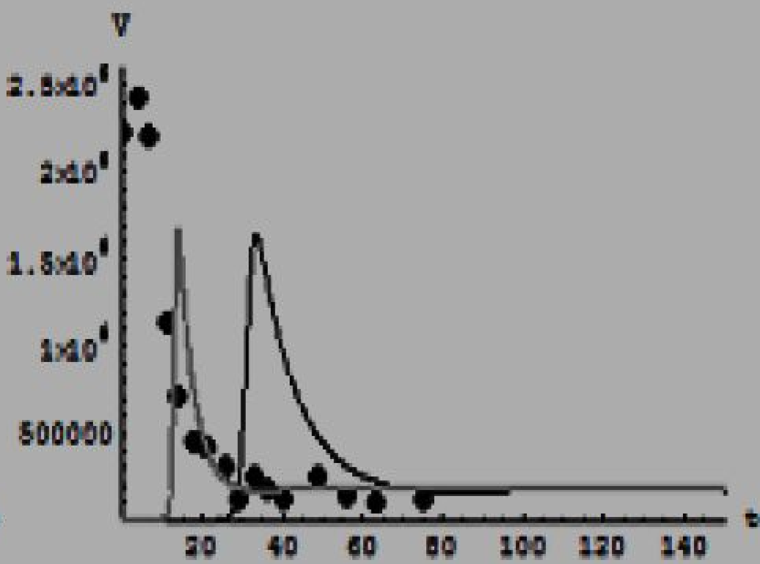
where $0 < \alpha_1, \alpha_2, \alpha_3, \alpha_4 \leq 1$, $T(t)$ is the density of uninfected target cells, $T^*(t)$ is the density of productively infected cells, $V(t)$ is the density of the free virus, and $E(t)$ is the density of the effector cells $E(t)$. The constant s represents a source of healthy cells and d is their death rate, k is the infection rate, and δ is the death rate of productively infected cells. The killing rate of infected cells by effector cells is represented by d_x. The inclusion of the term $d_x ET^*$, allows for the removal of productively infected T-cells due to a cell mediated immune response. N is the number of virions produced by an infected cell during its life span, and c is the viral clearance rate constant. Effector cells are assumed to be generated at a rate proportional to the level of productively infected cells, and die at a rate d_E [7, 20].

Table 1. The parameter values.

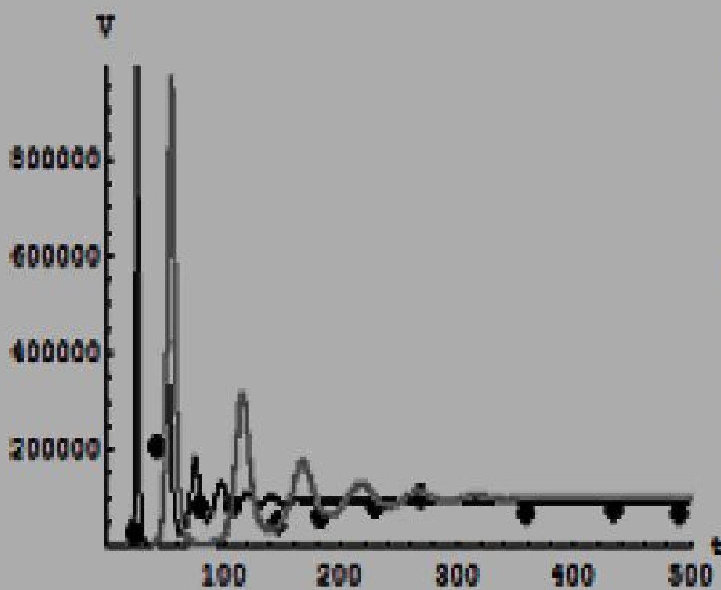
Patient	$d_x \times 10^{-4}$	p	d_E	N	d	$k \times 10^{-7}$	s	δ
1	2.2	0.07	0.01	5101	0.013	0.46	130	0.75
2	10	2	0.55	2966	0.02	3.6	200	0.80
3	5.4	0.01	0.02	5617	0.0065	6.4	65	0.10
4	6.8	0.01	4.07	668	0.0046	48	46	0.13
5	1.0	0.6	1.13	3843	0.017	6.3	170	0.22
6	7.2	2	2.13	1341	0.012	7.5	120	0.59
7	1.0	1	5.00	4493	0.017	8	170	0.32
8	1.0	0.01	0.97	6689	0.0085	6.6	85	0.10
9	1.0	0.01	2.87	1415	0.006	25	60	0.10
10	9.7	0.01	0.30	186210	0.0043	1.9	43	0.50



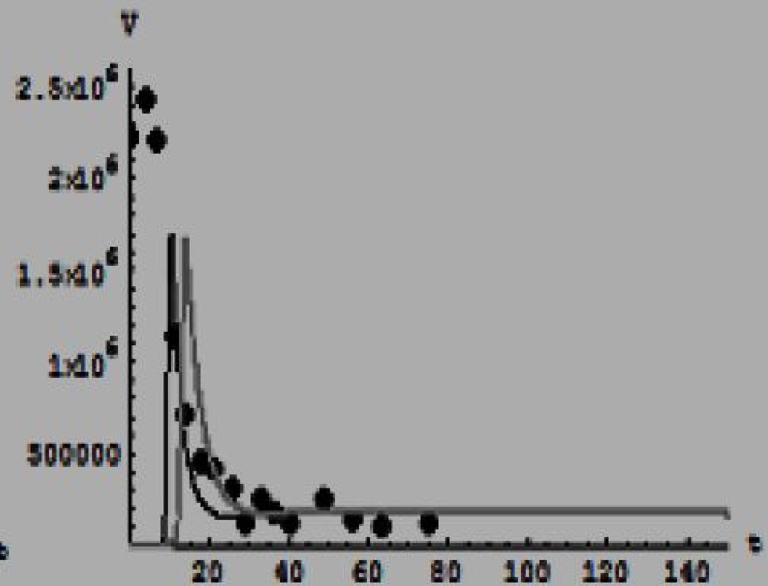
Patient 7 ($\alpha = 1$ (the black line), when $\alpha = 0.60$ (the gray line))



Patient 8 ($\alpha = 1$ (the black line), when $\alpha = 0.75$ (the gray line))



Patient 1 ($\alpha = 0.7$ (the black line), when $\alpha = 0.35$ (the gray line))



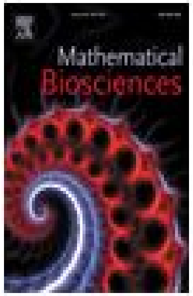
Patient 8 ($\alpha = 0.65$ (the black line), when $\alpha = 0.5$ (the gray line))

MODELS OF VECTOR BORNE DISEASES WITH MEMORY ON THE HOST AND THE VECTOR

ELSEVIER

Mathematical Biosciences

Volume 263, May 2015, Pages 18-36



A generic model for a single strain mosquito-transmitted disease with memory on the host and the vector

Tridip Sardar [a], Sourav Rana [b], Sabyasachi Bhattacharya [a], Kamel Al-Khaled [c, d], Joydev Chattopadhyay

MODELS OF VECTOR BORNE DISEASES WITH MEMORY ON THE HOST AND THE VECTOR

- Basically, the memory of human is closely related to the awareness.

- The memory of vector is related to their blood feeding behavior like detecting host location and host selection.

$$D^{\alpha}(S_H) = \mu_H(K - S_H) - \frac{b\beta_1 S_H I_V}{K},$$
$$D^{\alpha}(I_H) = \frac{b\beta_1 S_H I_V}{K} - (\mu_H + \gamma_H)I_H,$$
$$D^{\alpha}(R_H) = \gamma_H I_H - \mu_H R_H,$$
$$D^{\alpha}(S_V) = A - \frac{b\beta_2 I_H S_V}{K} - mS_V,$$
$$D^{\alpha}(I_V) = \frac{b\beta_2 I_H S_V}{K} - mI_V$$

Where $0 < \alpha \leq 1$, S_H, I_H and R_H are the populations of susceptible humans, infected human, and recovered human respectively. S_V and I_V are the populations of susceptible mosquitos, infected mosquitos. The total human population K at time t is denoted by N_H where $N_H = S_H + I_H + R_H$. The authors did not consider any recovered class in mosquito population because the life expectancy of mosquito is very short, so $N_V = S_V + I_V$.

T. Sardar, S. Rana, S. Bhattacharya, K. Al-Khaled, J. Chattopadhyay, A generic model for a single strain mosquito-transmitted disease with memory on the host and the vector, Math. Biosci. 263 (2015) 18–36.

MODELS OF VECTOR BORNE DISEASES WITH MEMORY ON THE HOST AND THE VECTOR

$$D^{\alpha}(S_H) = \mu_H^{\alpha}(K - S_H) - \frac{b^{\alpha}\beta_1 S_H I_V}{K},$$

$$D^{\alpha}(I_H) = \frac{b^{\alpha}\beta_1 S_H I_V}{K} - (\mu_H^{\alpha} + \gamma_H^{\alpha})I_H,$$

$$D^{\alpha}(R_H) = \gamma_H^{\alpha} I_H - \mu_H^{\alpha} R_H,$$

$$D^{\beta}(S_V) = A_2 - \frac{b^{\beta}\beta_2 I_H S_V}{K} - m^{\beta} S_V,$$

$$D^{\beta}(I_V) = \frac{b^{\beta}\beta_2 I_H S_V}{K} - m^{\beta} I_V.$$

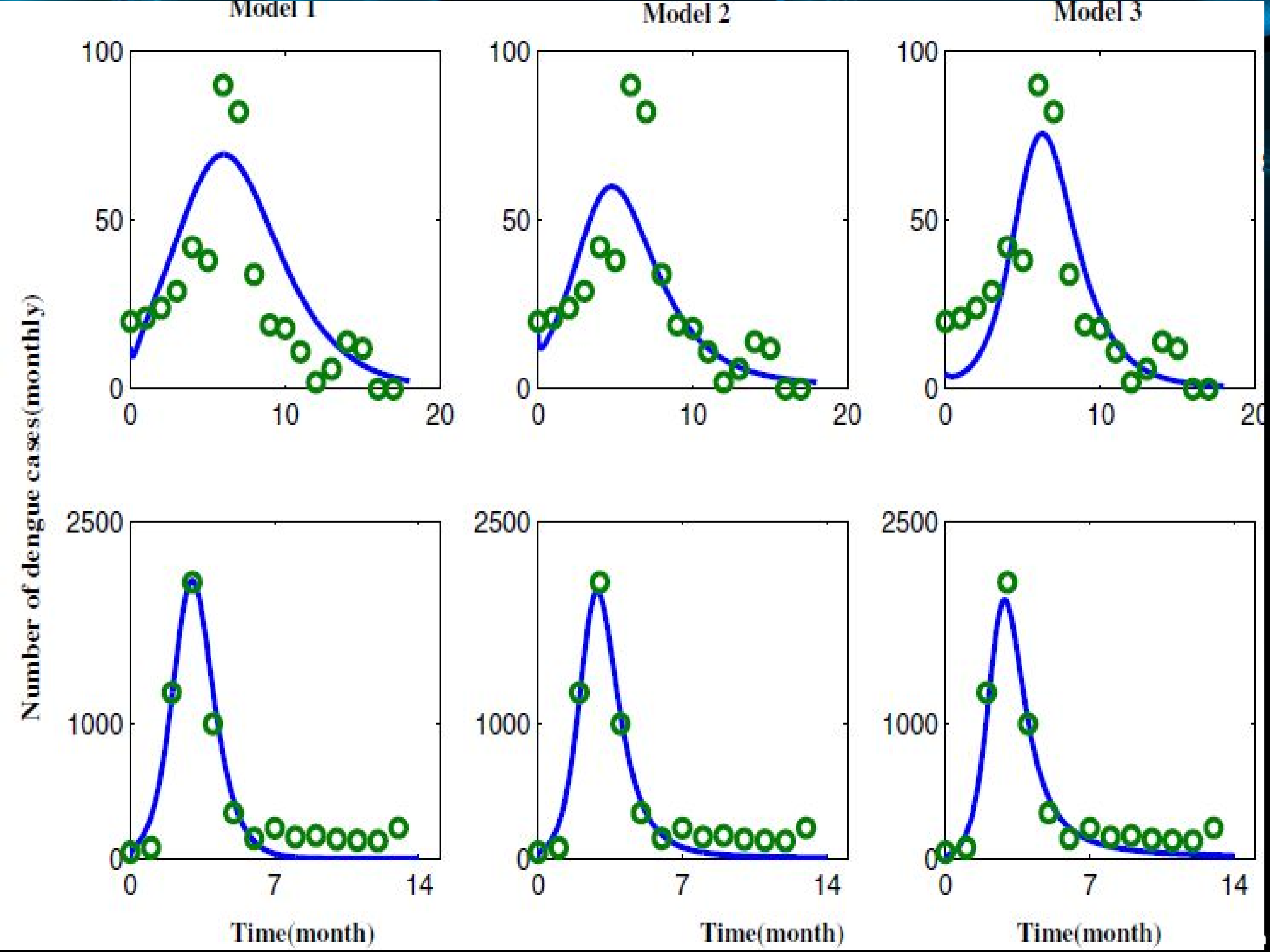
Where $0 < \alpha \leq 1$, $0 < \beta \leq 1$

THE BASIC REPRODUCTION NUMBERS

The infection persists if the basic reproduction number $R_0 > 1$, and dies out if $R_0 < 1$.

$$R_0 = \sqrt{\frac{b\beta_1}{m} \times \frac{b\beta_2 A}{mK(\mu_H + \gamma_H)}}$$

$$\overline{\overline{R}}_0 = \sqrt{\frac{b^\alpha \beta_1}{m^\beta} \times \frac{b^\beta \beta_2 A}{m^\beta K(\mu_H^\alpha + \gamma_H^\alpha)}}$$



Model 1
Model 2
Model 3
Number of dengue cases(monthly)
Time(month)
Time(month)
Time(month)

A VARIABLE FRACTIONAL ORDER NETWORK MODEL OF ZIKA VIRUS

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ISSN: 2090-5858.
http://fcag-egypt.com/Journals/JFCA/

A VARIABLE FRACTIONAL ORDER NETWORK MODEL OF ZIKA VIRUS

M. KHALIL , A. A. M. ARAFA , AMAAL SAYED

Variable Fractional Order Derivatives

(i) Left Caputo derivative of order $\alpha(t)$ is defined by

$$ {}_a^c D_t^{\alpha(t)} f(t) = \frac{1}{\Gamma(1-\alpha(t))} \int_a^t (t-\tau)^{-\alpha(t)} f'(\tau)\, d\tau, 0 < \alpha(t) \leq 1 $$

(ii) Right Caputo fractional order derivative of order $\alpha(t)$ is defined by

$$ {}_t^c D_b^{\alpha(t)} f(t) = \frac{-1}{\Gamma(1-\alpha(t))} \int_t^b (\tau-t)^{-\alpha(t)} f'(\tau)\, d\tau, 0 < \alpha(t) \leq 1 $$

A VARIABLE FRACTIONAL ORDER NETWORK MODEL OF ZIKA VIRUS

$$D^{\alpha_1(t)}S(t) = \lambda - \frac{\beta \langle k \rangle SI}{S+I+R} + \gamma R - (\delta + \mu)S,$$

$$D^{\alpha_2(t)}I(t) = \frac{\beta \langle k \rangle SI}{S+I+R} - (\varepsilon + \mu + \alpha)I,$$

$$D^{\alpha_3(t)}R(t) = \varepsilon I - (\mu + \gamma)R + \delta S,$$

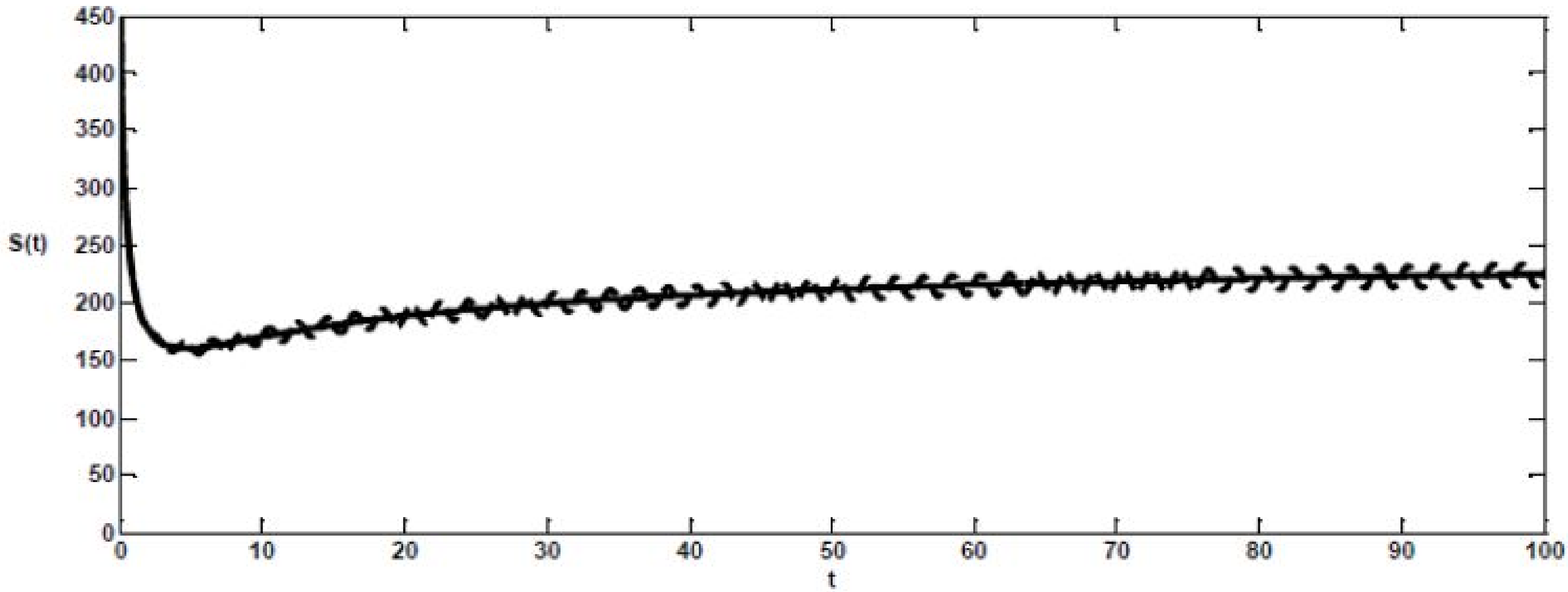


FIGURE 2. The dynamic trajectory $S(t)$ at $\alpha(t) = 0.7$ (the solid line) and at $\alpha(t) = 0.7 - 0.01sin(\pi t)$ (the dashed line)

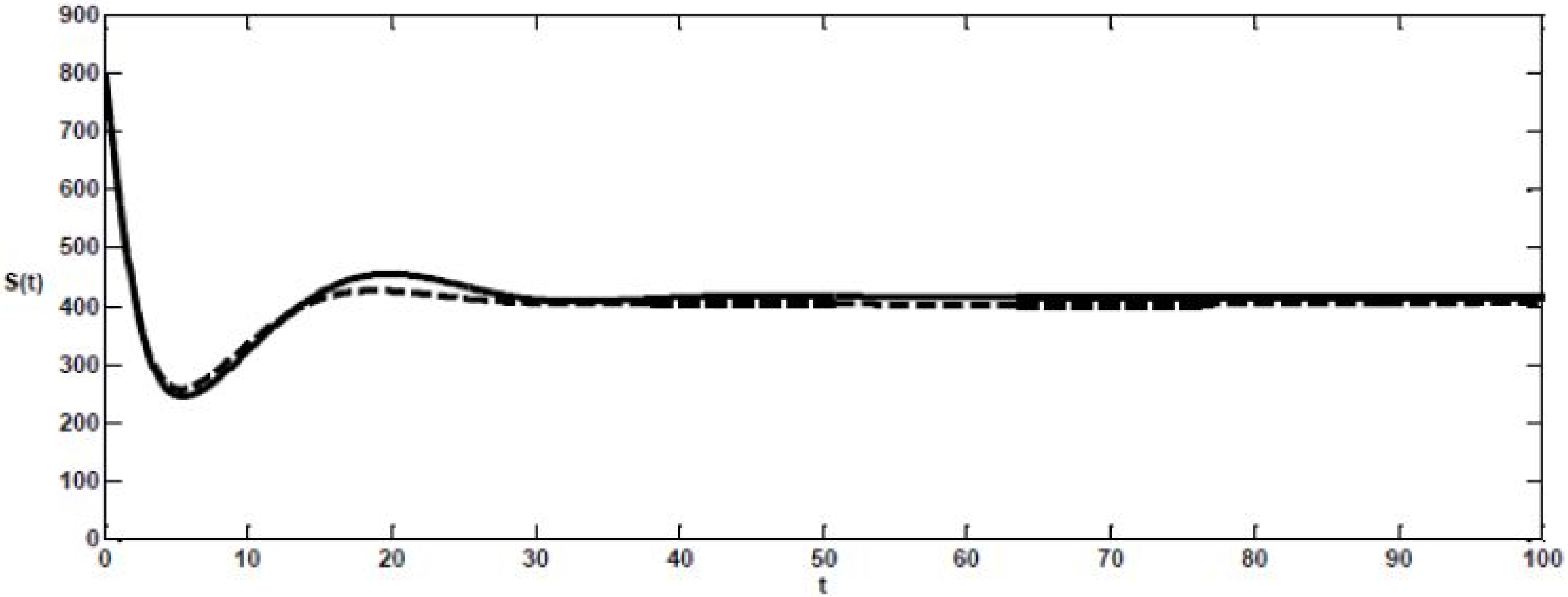


FIGURE 10. The dynamic trajectory $S(t)$ at $\alpha(t) = 1$ (the solid line) and at $\alpha(t) = 1 - 0.004t$ (the dashed line).

Numerical Solutions of Fractional Order Models

Applied Mathematical Modelling 37 (2013) 2189–2196

Contents lists available at SciVerse ScienceDirect

Applied Mathematical Modelling

journal homepage: www.elsevier.com/locate/apm

The effect of anti-viral drug treatment of human immunodeficiency virus type 1 (HIV-1) described by a fractional order model

A.A.M. Arafa [a,*], S.Z. Rida [a], M. Khalil [b]

[a] Department of Mathematics, Faculty of Science, South Valley University, Qena, Egypt
[b] Department of Mathematics, Faculty of Engineering, Modern Science and Arts University (MSA), Giza, Egypt

$$
\begin{aligned}
D^{\alpha_1}(x) &= s - \mu x - \beta x z,\\
D^{\alpha_2}(y) &= \beta x z - \varepsilon y,\\
D^{\alpha_3}(z) &= c y - \gamma z.
\end{aligned}
$$

The numerical results of $x(t)$.

t	GEM	HPM	HAM	RK4
0	100	100	100	100
0.2	100.023	100.023	100.023	100.023
0.4	100.047	100.047	100.047	100.047
0.6	100.071	100.071	100.071	100.071
0.8	100.097	100.097	100.096	100.097
1	100.122	100.123	100.122	100.122

The numerical results of $y(t)$.

t	GEM	HPM	HAM	RK4
0	0	0	0	0
0.2	0.00434	0.00434	0.004336	0.004336
0.4	0.00715	0.00721	0.007141	0.007154
0.6	0.00908	0.00934	0.009094	0.009081
0.8	0.01049	0.01117	0.010631	0.010492
1	0.01161	0.01276	0.011945	0.011610

The numerical results of $z(t)$.

t	GEM	HPM	HAM	RK4
0	1	1	1	1
0.2	0.69030	0.69071	0.69059	0.69070
0.4	0.51152	0.51208	0.51237	0.51190
0.6	0.41069	0.41394	0.40994	0.41103
0.8	0.35656	0.37749	0.35148	0.35684
1	0.33053	0.42419	0.32869	0.33073

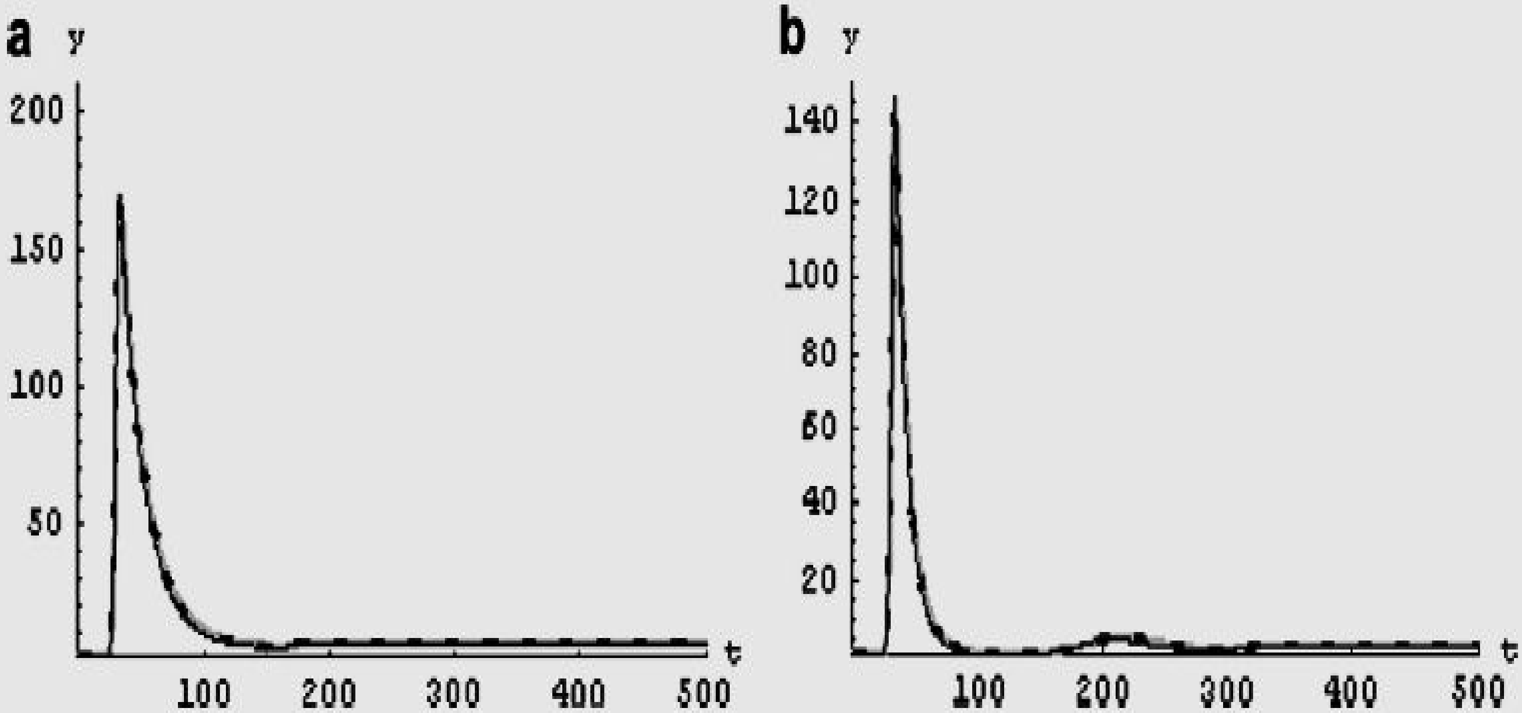
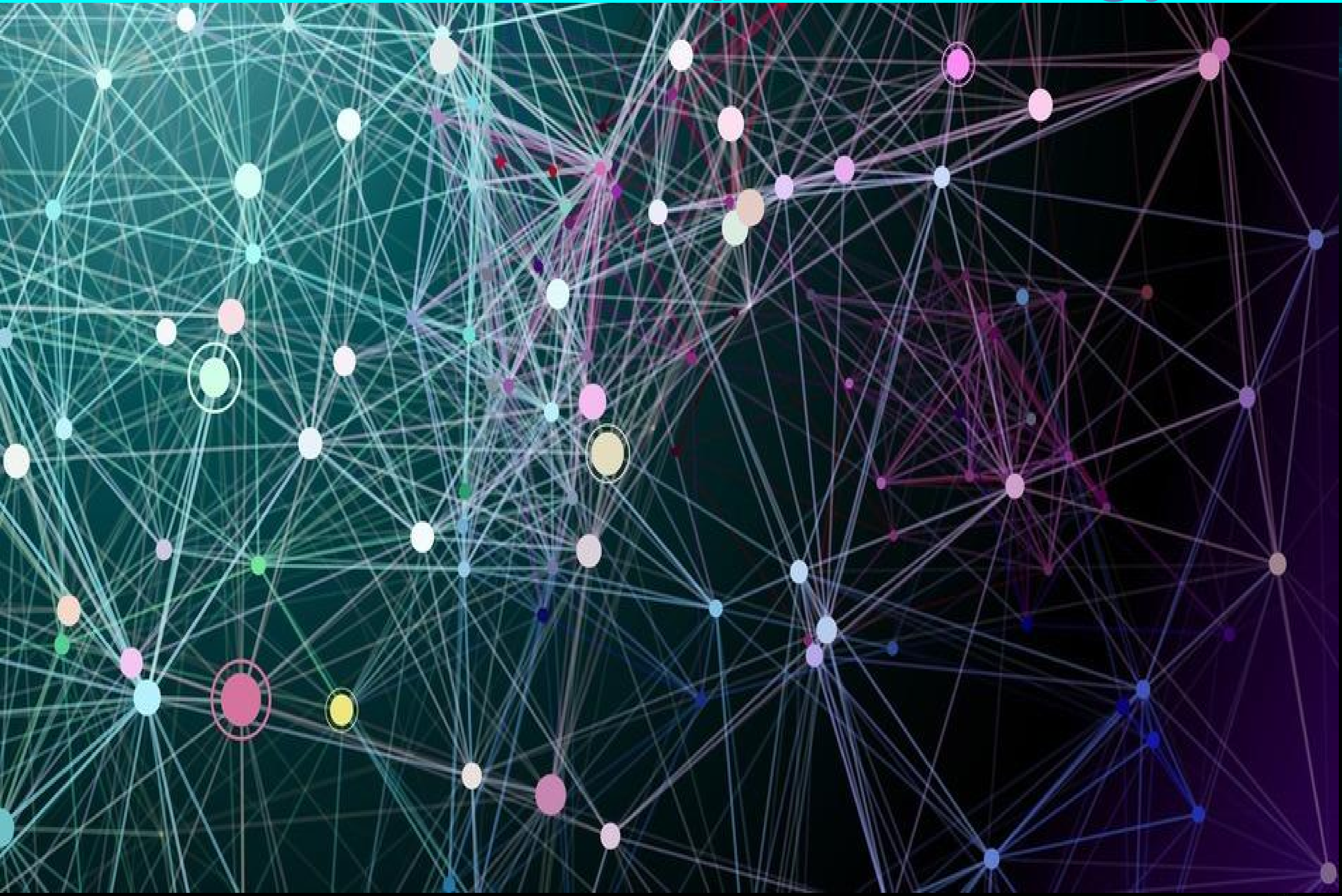


Fig. 2. The densities of the infected CD4[+] T-cells $y(t)$, when $\varepsilon = 0.1$ (a), and $\varepsilon = 0.05$ (b): gray solid line ($\alpha = 1$), dotted line ($\alpha = 0.99$), black solid line ($\alpha = 0.95$).

Future work

Networks in Epidemiology



Big Data Mathematical Modeling in Epidemiology

Thank you for listening ☺