Modeling and Simulation of Viral strain growth

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***Abstract*—The basic idea of this project is to implement and analyze various Numerical Integration and Model Order Reduction techniques on a simulated model of Viral Strain evolution**

I. Introduction & Motivations

The growth of viral strains is of interest in the field of vaccine design. We carried out a brief study of how we can simulate the system and analyze it efficiently using various Model Order Reduction techniques

II. Problem formulation

Every viral strain in has three parameters associated with it

1) Replication rate: The rate of replication of a strain with time
2) Death rate: The rate of death of a strain with time owing to competition
3) Mutation rate: The rate of change of one strain into another with time

Our nodal quantities are the concentrations of the individual strains and these change with time in accordance with the parameters described above. Let

$x_i(t)$ = Concentration of the i-th strain
R_i = Replication rate of the i-th strain
D_i = Replication rate of the i-th strain
μ_{ij} = Mutation rate from i-th to j-th strain
The evolution is described by the equation

$$\frac{dx_i(t)}{dt} = \left\{(R_i - D_i) - \sum_{j \neq i} \mu_{ij} R_i + \sum_{j \neq i} \mu_{ji} R_j \right\} x_i(t) \quad (1)$$

This can be converted into state space form as

$$\frac{d\mathbf{x}(t)}{dt} = \mathbf{A}\mathbf{x}(t) + \mathbf{B}u(t)$$
$$y(t) = \mathbf{C}\mathbf{x}(t) + \mathbf{D}u(t)$$

Where

$$\mathbf{A} = \begin{bmatrix} R_1 - D_1 & \mu_{1,2} & \cdots & \mu_{1,N} \\ \mu_{2,1} & R_1 - D_1 & \cdots & \mu_{2,N} \\ \vdots & \vdots & \ddots & \vdots \\ \mu_{N,1} & \mu_{N,2} & \cdots & R_N - D_N \end{bmatrix}$$

$$B = [1 \;\; 1 \;\; \cdots \;\; 1 \;\; 1]'$$
$$C = [0 \;\; 0 \;\; \cdots \;\; 0 \;\; 1]$$
$$D = [0]$$

Here u(t) is a constant which represents the amount of the viral strains introduced into the population. $\mathbf{B}$ denotes the relative contribution of the introduced strains. $\mathbf{C}$ denotes the strain of interest, which in this case is the strain with the highest fitness

III. Numerical Techniques

The first task was to compute the time evolution of the viral population. For this we explored three Numerical Integration techniques

1) Forward Euler Approximation
2) Backward Euler Approximation
3) Trapezoidal Rule Approximation

We also implemented a computationally faster Backward Euler Approximation in which we used different time steps depending on the dynamics of the system.

We applied three model order reduction techniques as well, namely

1) Singular Value Decomposition
2) Truncated Balanced Realization
3) Krylov Subspace Analysis

IV. Results

First we verified the instability point of the Forward Euler Approximation. We then did a comparison of the timing (Figure IV) and error performance (Figure IV) of the various integration techniques. We found out that the Forward Euler Approximation best suited our problem within the timing and error bounds.

Next we moved on to the model order reduction techniques and were able to successfully reduce the execution time multiple times (Figure IV) with a small sacrifice in the error performance (Figure IV).

References

[1] Domingo E, Sheldon J, Perales C. Viral Quasispecies Evolution. *Microbiology and Molecular Biology Reviews: MMBR.* 2012;76(2):159-216. doi:10.1128/MMBR.05023-11.

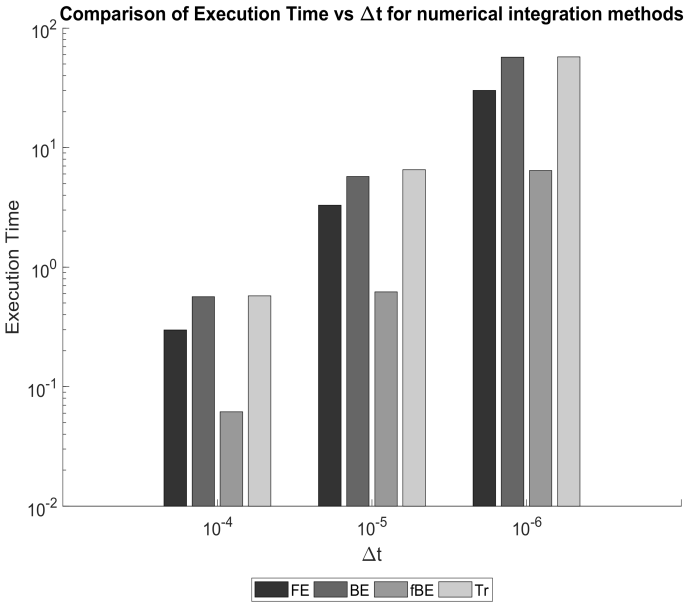

Fig. 1.

Fig. 3.

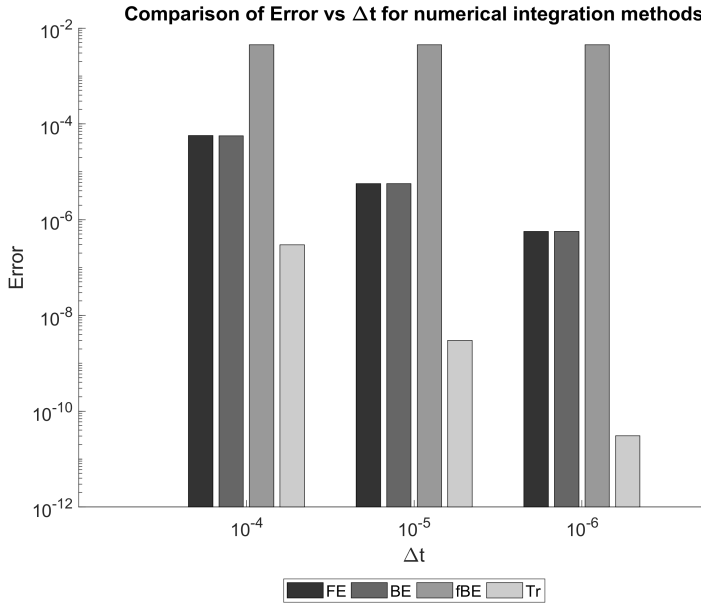

Fig. 2.

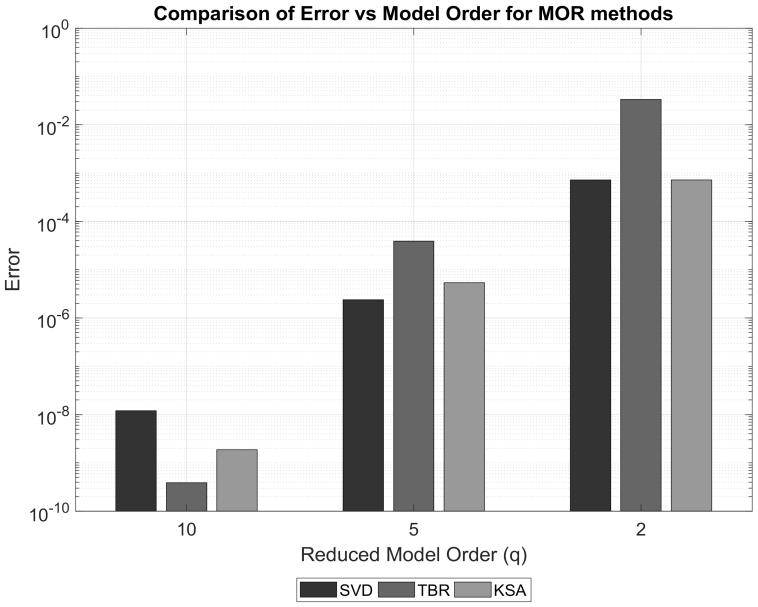

Fig. 4.