Chaos ARTICLE pubs.aip.org/aip/cha

Threshold dynamics and epidemic-informed machine learning for forecasting of mpox: A U.S. case study

Cite as: Chaos **35**, 113118 (2025); doi: 10.1063/5.0299032
Submitted: 25 August 2025 · Accepted: 18 October 2025 ·
Published Online: 13 November 2025

View Online Export Citation CrossMark

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Note: This paper is part of the Special Topic on Nonlinear Dynamics, Network Science, and Machine Learning: Dedicated to Ljupco Kocarev's 70th Birthday.

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ABSTRACT

Mpox (monkeypox) is a re-emerging viral disease with increasingly sustained human transmission, particularly in previously unaffected regions. In this study, we develop a compartmental epidemic model that captures mpox transmission dynamics and incorporates a treatment function to assess the impact of medical interventions on disease progression and recovery. The model is calibrated using U.S. case data, with parameters estimated via the Trust Region Reflective optimization method to ensure close alignment with observed trends. We perform global sensitivity analysis using partial rank correlation coefficients to identify key parameters influencing transmission. The model's bifurcation structure is examined through the basic reproduction number R_{M0}, revealing both forward and backward bifurcations that highlight threshold behavior and the potential for complex endemic dynamics. For real-time forecasting, we incorporate prior knowledge of mpox dynamics into machine learning models, ARNN (Autoregressive Neural Network), ARIMA (Autoregressive Integrated Moving Average), and LSTM (Long Short-Term Memory), achieving improved predictive accuracy over traditional methods. These epidemic-informed models benefit from mechanistic insights, enhancing their responsiveness to changing trends. Our results emphasize the importance of timely treatment, hygiene, and vaccination in mitigating mpox spread. The integrated modeling and the forecasting framework provide valuable tools for anticipating outbreaks and informing public health strategies.

In recent years, mathematical modeling has played a central role in understanding the transmission dynamics of emerging infectious diseases. This article develops and analyzes a compartmental model for mpox that incorporates human-to-human transmission and an environmental reservoir. The model is explored through threshold analysis, bifurcation theory, and sensitivity studies to identify the key drivers of disease spread. Beyond mechanistic insights, we extend the study to epidemic-informed time series forecasting, integrating machine learning and deep learning techniques to enhance predictive accuracy. This dual framework provides a novel approach that links rigorous dynamical analysis with data-driven forecasting, offering practical implications for public health interventions and outbreak control.

I. INTRODUCTION

Mpox (Monkeypox) has emerged as a significant global public health concern, necessitating integrated methodological frameworks to understand, model, and mitigate its spread. Caused by the mpox virus (MPXV), a member of the *Orthopoxvirus* genus that also includes the variola virus (smallpox), the disease manifests with symptoms, such as fever, rash, lymphadenopathy, and myalgia. In severe cases, complications may include secondary infections and respiratory distress.[1,2] While initially associated with zoonotic spillover, current evidence indicates that human-to-human transmission is now the primary mode of spread, facilitated through close physical contact, respiratory droplets, exposure to skin lesions, and contaminated environments.[3,4]