frontiers in Applied Mathematics and Statistics

TYPE Editorial
PUBLISHED 28 May 2026
DOI 10.3389/fams.2026.1869506

OPEN ACCESS

EDITED AND REVIEWED BY
Koyel Chakravarty,
SRM University AP, India

*CORRESPONDENCE
Joseph Malinzi
josephmalinzi@aims.ac.za

RECEIVED 30 April 2026
ACCEPTED 13 May 2026
PUBLISHED 28 May 2026

CITATION
Malinzi J and Byrne HM (2026) Editorial: Quantitative insights into new cancer therapies: a mathematical modeling approach.
Front. Appl. Math. Stat. 12:1869506.
doi: 10.3389/fams.2026.1869506

Editorial: Quantitative insights into new cancer therapies: a mathematical modeling approach

Joseph Malinzi[1,2]* and Helen M. Byrne[3,4]

[1]Department of Mathematics, Faculty of Science and Engineering, University of Eswatini, Kwaluseni, Eswatini, [2]Institute of Systems Science, Durban University of Technology, Durban, South Africa, [3]Wolfson Centre for Mathematical Biology, Mathematical Institute, University of Oxford, Oxford, United Kingdom, [4]Ludwig Institute for Cancer Research, Nuffield Department of Medicine, Oxford, United Kingdom

KEYWORDS
agent-based models, cancer modeling, causal inference, equation learning, immunotherapy, mathematical oncology, oncolytic virotherapy, sequential treatments

Editorial on the Research Topic
Quantitative insights into new cancer therapies: a mathematical modeling approach

Introduction

The development of new anti-cancer therapies is time-intensive and costly, and traditionally relies on extensive laboratory and clinical experimentation. To complement these efforts, mathematical and computational approaches are increasingly used to address key research questions, reduce experimental burden, and guide decision-making. In oncology, a range of emerging treatment modalities—including immunotherapy, gene therapy, targeted therapies, nanomedicine, and oncolytic virotherapy—represent a significant shift toward more precise and personalized cancer care. These approaches are designed to preferentially target cancer cells while limiting damage to healthy tissue, often by engaging or enhancing the body's own immune response. Mathematical modeling offers a unifying framework for studying the complex, multi-scale interactions between tumors, therapies, and the immune system. By integrating experimental and clinical data, such models enable the simulation, analysis, and optimization of treatment strategies, while also helping to identify biological constraints and practical challenges related to therapy delivery. As such, modeling serves as a critical bridge between experimental research and clinical application, supporting collaboration across disciplines [1].

Figure 1 provides a visual roadmap for the argument developed in this editorial. We propose that the four articles in this Research Topic are not isolated contributions but exemplars of a broader, unified pipeline. This pipeline begins with the recognition that current clinical practice faces structural limitations—costly trials, one-size-fits-all dosing, and static protocols, among others—which create demand for quantitative approaches. The central hub, mathematical modeling, supplies a diverse toolkit from which five therapeutic paradigms emerge, defining a future vision for oncology. A dashed feedback loop completes

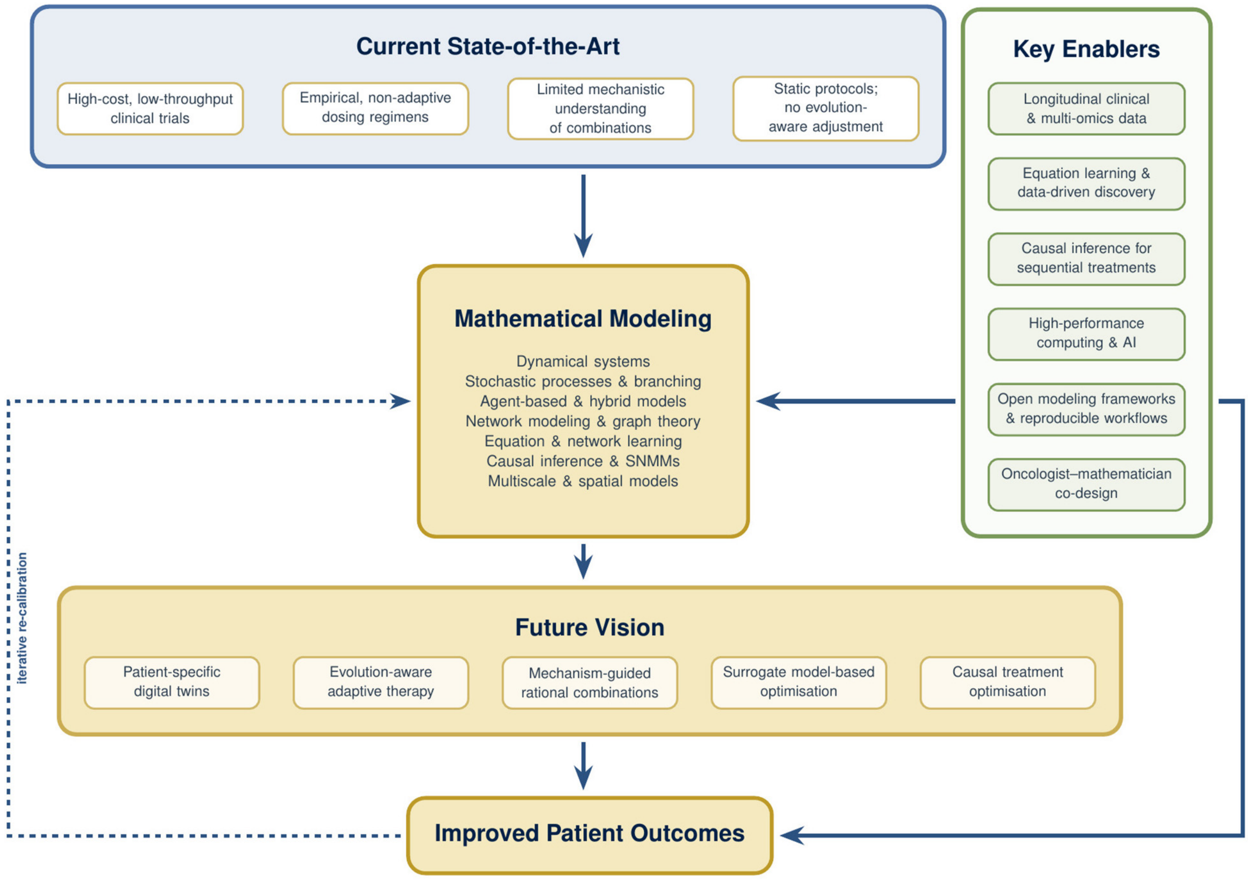

FIGURE 1
Conceptual pipeline from current limitations in cancer therapy to improved patient outcomes, mediated by mathematical modeling. The top-left panel (*Current State-of-the-Art*) identifies structural barriers to evidence-based treatment design. These motivate the central hub (*Mathematical Modeling*), which integrates complementary quantitative frameworks that translate biological complexity into testable predictions. This Research Topic showcases several such frameworks: Bansod and Hillen, Burrage et al., Kim, and Liao et al. The right column (*Key Enablers*) specifies the infrastructure and tools needed for translation. The lower band (*Future Vision*) outlines therapeutic paradigms enabled by mathematical modeling, culminating in *Improved Patient Outcomes*. The dashed arrow signifies iterative model recalibration as clinical data accumulate.

the cycle, underscoring that models must be continually recalibrated as new clinical data accrue.

This Research Topic aims to increase understanding of how mathematical modeling can serve as a pivotal tool in the evolution of cancer treatment. Specific goals include optimizing existing treatment strategies, closely examining the dynamics of emerging therapies, elucidating their impact on tumor growth, and predicting responses to different treatment modalities. Through various modeling techniques such as ordinary differential equations and agent-based modeling, this topic seeks to illuminate the intricate mechanisms of action of these therapies and facilitate the development of improved treatment protocols. The Research Topic includes contributions that develop and simulate mathematical models to predict treatment efficacy, explore inter-treatment interactions within a mathematical framework, analyze the influence of the tumor microenvironment on treatment outcomes, optimize treatment schedules and dosage plans, and construct and validate models that predict outcomes of combination therapies. Importantly, the articles focus on robust model validation, precise parameter estimation, the utilization of models in clinical or virtual trials, and strategies for integrating multiple treatment modalities.

Overview of contributions

Understanding the complexity of cancer treatment necessitates multiscale approaches that can capture both stochastic cellular dynamics and deterministic population-level behaviors. The four articles in this Research Topic illustrate the breadth of mathematical modeling approaches that can be used to address these challenges, each focusing on different aspects of cancer therapy: from viral dynamics and spatiotemporal pattern formation to surrogate model construction, evolutionary principles, and causal statistical inference. Table 1 provides a structured summary of each contribution and an editorial commentary on its methodological significance and clinical relevance.

Bansod and Hillen analyse the spatiotemporal dynamics of oncolytic virotherapy using a reaction-diffusion model that couples

TABLE 1 Summary of contributions: models, methods, key results, and editorial comment.

Study	Methods	Key results	Editorial comment
I. Bansod and Hillen	Center-manifold reduction near the Hopf threshold incorporating nonlinear terms; near-identity normal form transformation yielding the Stuart-Landau equation; spatial extension to the Complex Ginzburg-Landau Equation (CGLE). The asynchrony parameter β is estimated numerically from ODE eigenvalues and the measured oscillation period.	Prior experimentally observed tumor patterns (hollow rings, concentric rings, fragmented aggregates) are shown to emerge from the Hopf bifurcation mechanism and evolve naturally toward spiral waves and turbulence, confirming they are intrinsic system features rather than numerical artifacts. The C-I-V system operates at $\beta \approx 40$, placing it within the turbulent regime. Complete tumor eradication via oncolytic monotherapy remains unreliable even with substantially increased viral replication rates.	A technically rigorous reduction brings analytical clarity to a complex class of models. The derivation of β from measurable kinetic quantities is elegant and practically useful. The demonstration that turbulence is intrinsic rather than parameter-dependent provides a strong theoretical basis for the clinical observation that oncolytic monotherapy alone has limited efficacy.
II. Burrage et al.	Coupled equation learning using a constrained library of 49 chemical reactions under the Law of Mass Action. Non-negative least-squares optimization selects a sparse reaction set. A union model is constructed across six scenarios, with an RMSE-based hyperparameter scan over differentiation scheme and sampling frequency used to identify the optimal configuration.	Twelve reactions suffice to reproduce six ABM scenarios (mean RMSE $\approx 5.45 \times 10^{-3}$). A linear relationship holds between steady-state cancer density and initial immune cell fraction. For a competition value $C_I = 0.5$, reducing the cancer density from its baseline steady-state level (≈ 0.88) to $C^* = 0.2$ requires an initial immune fraction $\tilde{I}(0) \approx 0.946$. With a stronger competition value $C_I = 0.75$, the same cancer reduction requires only $\tilde{I}(0) \approx 0.658$.	The construction of an interpretable surrogate ODE from a stochastic spatial model is a significant methodological contribution. The linearity result provides an actionable insight that bridges rigorous modeling and clinical protocol design. The union-model construction across multiple scenarios, rather than fitting to a single trajectory, guards against overfitting and strengthens confidence in the surrogate's generalizability.
III. Kim	Maximum-likelihood estimation of Ornstein-Uhlenbeck parameters (μ, θ, σ) via replicate-grouped exact transition likelihood. Nonparametric bootstrap ($B = 2,000$) for uncertainty quantification. Two-dimensional profile-likelihood surfaces in (θ, σ) space. Forward simulations with phenotype-coupled birth-death rates; illustrative cyclic therapy simulation under the *priA* parameter profile coupled to a pharmacokinetic exposure function.	Three distinct evolutionary regimes are identified: stabilized (wild-type), hypermutable/plastic (*priA*), and collapse-prone (*recG*). The *priA* lineage is separated from *recG* by approximately 88-fold in mutation frequency. Cyclic therapy simulations generate oscillatory suppression-rebound dynamics and clonal pruning, producing testable hypotheses for evolution-aware treatment scheduling.	This contribution draws a rigorous analogy between bacterial DNA-repair mutants and pediatric tumor subclones. The likelihood-based inference is thorough, and the uncertainty quantification is careful. The framing of the *priA* lineage as an analo for hypermutable tumor subclones is generative, though direct validation in patient data remains for future work. The unified stochastic approach offers a valuable framework for moving beyond deterministic treatment models.
IV. Liao et al.	The method standardizes point effects (single-treatment effects) to a small number of scientifically motivated strata, which removes the requirement for explicit treatment assignment conditions. These standardized point effects are then regressed onto basis functions of a Structural Nested Mean Model (SNMM) to estimate the blip effect vector γ. Bootstrap covariance estimation incorporates variability from all treatments and covariates, and a Wald test is used for hypothesis testing. A simulation study validates the approach for three outcome types: Gaussian, Bernoulli, and Poisson.	The method achieves unbiased estimates and nominal 95% coverage across all three outcome distributions and both SNMM specifications. Imposing cross-time SNMM constraints substantially reduces variance and increases power relative to unconstrained alternatives. Clinically, patients aged under 60 benefit from large diagnosing hospitals, while those aged over 68 benefit from large treating hospitals, revealing a clear age-modification signal.	A statistically sophisticated contribution, deserving attention beyond mathematical oncology. The key insight, that standardization of point effects can replace the need for treatment assignment conditions, is theoretically sound and practically useful for analyzing observational sequential treatment data. The medical example is well chosen: the age-modification finding is clinically plausible and would be difficult to detect reliably with existing methods.

uninfected tumor cells, infected tumor cells, and free virus particles. By applying a center-manifold reduction to a classical cell-infection-virus (C-I-V) model, they derive a complex Ginzburg–Landau equation whose parameters depend on the underlying biological kinetics. Their analysis shows that spatial patterns previously observed in such models (e.g., rings and fragmented structures) evolve over longer timescales into spiral waves and turbulent dynamics, originating from a Hopf bifurcation in the reaction kinetics. The authors identify the asynchrony parameter as the key determinant of pattern stability and demonstrate that biologically relevant parameter values place the system within the turbulent regime. These findings establish spatiotemporal complexity as an intrinsic feature of oncolytic virotherapy and suggest fundamental limits on tumor eradication by viral monotherapy alone.

Burrage et al. extend a two-species agent-based model of cancer to include immune cells (T-cells). They apply coupled equation learning to the resulting three-species model via a library of chemical reactions under the Law of Mass Action to construct a population-based surrogate reaction model. They simulate six scenarios which differ in terms of the initial immune cell concentration and the strength of the competition between cancer cells and immune cells. The authors show how the six individually learned models can be unified into a single surrogate population-based model which comprises three coupled ordinary differential equations that are markedly easier to analyze than the original agent-based model. As a key analytical result, by identifying the unique positive equilibrium solution for the cancer concentration from the learned ODE system, they establish a linear relationship between the steady-state cancer concentration and the initial concentration of immune cells. This relationship is confirmed across both competition values, and enables estimation of values for the competition parameter and the initial immune cell concentration that will reduce the cancer to clinically acceptable levels without performing extensive agent-based simulations. The authors show that the equilibrium cancer cell density decreases with increasing initial immune cell fraction and with increasing immune cell competitive strength, demonstrating that combining a larger initial immune cell dosage with greater competitive ability yields compounded therapeutic benefit.

Kim presents a hybrid modeling framework that combines stochastic trait evolution with birth–death population dynamics to study lineage diversification under stabilizing selection and random drift. The model is calibrated using long-term evolution data from three *Escherichia coli* lineages (wild-type, priA, and recG), allowing estimation of key parameters governing typical trait values, variability, and the strength of stabilizing forces. This approach distinguishes three evolutionary regimes: stable behavior in the wild-type, highly variable and plastic dynamics in priA, and instability with frequent collapse in recG. The priA lineage, characterized by high variability and weak stabilization, is proposed as an analog for hypermutable tumor subclones that can drive pediatric cancer relapse despite low mutation burdens, while recG resembles fragile lineages under replication stress. Illustrative treatment simulations based on the priA regime show how cyclic therapy can produce oscillatory traits, suppression–rebound dynamics, and clonal loss. These simulations are presented as hypothesis-generating, with the framework designed for future calibration to longitudinal clinical data to enable evolution-aware, patient-specific modeling.

Liao et al. address causal inference challenges in longitudinal studies where treatments are assigned sequentially and time-varying covariates are influenced by earlier treatments. This feedback may confound the choice of subsequent treatments, posing significant difficulties for standard methods. The authors propose an approach based on using standardized point effects to estimate blip effects, defined as the net causal effect of a treatment on the outcome when all subsequent treatments are set to control. Their key innovation is to group point-treatment effects into a small number of scientifically motivated strata, enabling efficient regression estimation of structural nested mean model (SNMM) parameters without requiring restrictive treatment assignment assumptions. The method is illustrated using a medical study of 1,067 stomach cancer patients, examining how diagnosis and treatment in large vs. small hospitals affect 1-year survival and how these effects vary with age. A simulation study, using treatment sequences of length $T = 3$ with normal, dichotomous, and Poisson outcomes, confirms unbiased estimates, nominal coverage probability, and high statistical power. Indeed, their approach matches the performance of methods that require treatment assignment conditions while offering greater flexibility for targeted analysis and cross-time SNMM constraints.

Conclusion

Collectively, these four articles showcase the ability of mathematical modeling to increase understanding of complex cancer dynamics and its potential to identify optimal therapeutic strategies. From pattern formation in virotherapy and surrogate modeling of immune interactions to evolutionary principles in pediatric tumors and statistical methods for sequential treatments, this Research Topic advances our quantitative understanding of cancer therapy. The methodological diversity, encompassing bifurcation analysis and amplitude equation reduction, equation learning, hybrid stochastic branching processes, and causal inference for longitudinal data, reflects the multifaceted nature of cancer research and the necessity of interdisciplinary approaches. Each contribution identifies key parameters governing treatment outcomes: the asynchrony parameter that controls viral spread patterns, the competition value and initial immune cell dosage required to reduce cancer to manageable levels, the stabilizing strength and diffusion scale governing tumor evolutionary plasticity, and the blip effects of sequential treatment decisions modifiable by patient age. As these contributions demonstrate, mathematical modeling not only supplements clinical trials but also generates testable hypotheses, identifies key parameters governing treatment outcomes, and provides principled frameworks for personalized medicine. We hope this Research Topic inspires further collaboration between mathematicians, oncologists, and clinicians, accelerating the translation of quantitative insights into improved cancer care.

Author contributions

JM: Visualization, Writing – review & editing, Writing – original draft, Conceptualization. HB: Writing – original draft, Visualization, Writing – review & editing, Conceptualization.

Acknowledgments

We thank all authors and reviewers who contributed to this Research Topic, and the editorial staff at Frontiers in Applied Mathematics and Statistics for their support. JM is grateful to the Africa Oxford Initiative (AfOx) for supporting his two research visits to the University of Oxford, where he was hosted by Professor Helen Byrne, and to the Sydney Mathematical Research Institute (SMRI) for supporting his research visit there.

Conflict of interest

The author(s) declared that this work was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Generative AI statement

The author(s) declared that generative AI was used in the creation of this manuscript. AI was used exclusively to rephrase select statements. All ideas, arguments, and conclusions originate with and were verified by the author(s).

Any alternative text (alt text) provided alongside figures in this article has been generated by Frontiers with the support of artificial intelligence and reasonable efforts have been made to ensure accuracy, including review by the authors wherever possible. If you identify any issues, please contact us.

Publisher's note

References

1. Malinzi J, Basita KB, Padidar S, Adeola HA. Prospect for application of mathematical models in combination cancer treatments. *Inform Med Unlocked.* (2021) 23:100534. doi: 10.1016/j.imu.2021.100534