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Computational Systems Biology Models for Regenerative Pathway Simulation

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ABSTRACT

Regenerative biology is governed by interlocking molecular signalling pathways -- Wnt, Notch, TGF-beta, Hedgehog, mTOR, and their downstream effectors -- whose dynamic interactions determine the balance between stem cell self-renewal and differentiation, tissue repair and fibrosis, and regenerative success and failure. Computational systems biology modelling of these pathways -- using ordinary differential equation (ODE) models, Boolean network models, and agent-based simulations -- provides a mechanistic framework for understanding pathway dynamics and predicting the effects of perturbations (genetic mutations, drug treatments, microenvironmental signals) on regenerative outcomes. This paper proposes the Regenerative Pathway Simulation Systems Biology (RPSSB) framework, a multi- formalism computational systems biology methodology for simulation of regenerative signalling pathways, comprising five modelling components: an ODE kinetic model builder (OKB) for quantitative signalling dynamics; a Boolean network regeneration simulator (BNRS) for qualitative pathway state analysis; a multi-scale agent-based tissue regeneration simulator (MABRS) integrating cell-level and tissue-level dynamics; a parameter estimation engine (PEE) fitting model parameters to experimental time-course data; and a perturbation response predictor (PRP) simulating the effect of genetic or pharmacological perturbations on regenerative pathway output. RPSSB is evaluated across four regenerative pathway systems: Wnt-Notch crosstalk in intestinal stem cell renewal, TGF-beta/Smad fibrosis-regeneration balance in liver, mTOR pathway regulation of satellite cell activation in skeletal muscle, and Hedgehog-mediated chondrocyte differentiation in cartilage. OKB reproduces experimental time-course data with mean R2 = 0.924 (SD = 0.028) across four pathway systems. BNRS identifies 84.6% of known stable regenerative and fibrotic attractor states. PRP predicts drug perturbation effects with AUC = 0.918 (SD = 0.022). MABRS simulations reproduce tissue-level regeneration dynamics with r = 0.884 (SD = 0.028) vs. experimental histological time-course data. The study contributes the RPSSB specification, four calibrated regenerative pathway models, and a ranked catalogue of 128 computationally predicted therapeutic perturbation strategies.

Keywords: systems biology; regenerative pathways; ODE modelling; Boolean networks; agent-based simulation; Wnt; TGF-beta; parameter estimation; perturbation prediction

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1. Introduction

1.1 Systems Biology of Regenerative Pathways

The molecular machinery of tissue regeneration is not a collection of independent pathways but a highly interconnected signalling network in which pathway crosstalk, feedback loops, and non-linear signal integration collectively determine regenerative outcomes. Wnt signalling promotes stem cell self-renewal but is antagonised by Notch in the intestinal crypt, creating a lateral inhibition pattern that spatially organises stem cell identity (Clevers, 2013). TGF-beta promotes fibrosis through Smad2/3 activation but simultaneously suppresses inflammatory signalling through Smad7, creating context-dependent pro- and anti-regenerative effects (Massague, 2012). mTOR integrates nutrient, growth factor, and injury signals to regulate satellite cell activation (Mounier et al., 2011) but chronic mTOR hyperactivation impairs autophagy-dependent tissue quality control. These pathway-level complexities cannot be understood intuitively from linear pathway diagrams -- they require computational modelling that explicitly represents the dynamic interactions, feedback structures, and parameter dependencies of the network. The RPSSB framework provides a multi- formalism systems biology toolkit -- combining the quantitative precision of ODE kinetic models, the scalability of Boolean networks, and the spatial realism of agent-based simulations -- for comprehensive regenerative pathway analysis.

1.2 Research Contributions and Structure

This paper proposes RPSSB with five components (OKB, BNRS, MABRS, PEE, PRP) and four calibrated pathway models. Key contributions: OKB R2 = 0.924; BNRS identifies 84.6% of known attractors; PRP AUC = 0.918; MABRS r = 0.884 vs. histological time-course; 128 perturbation strategy catalogue. Section 2 reviews computational systems biology for regeneration. Section 3 presents RPSSB. Section 4 describes pathway models and evaluation. Section 5 reports results. Section 6 discusses implications. Section 6 concludes.

2. Background and Related Work

2.1 ODE and Boolean Modelling in Systems Biology

ODE kinetic models represent signalling pathway dynamics as systems of differential equations where molecular species concentrations change according to biochemically motivated rate laws (mass action, Michaelis-Menten, Hill function kinetics). ODE models of Wnt signalling (Lee et al., 2003), TGF-beta/Smad (Schmierer et al., 2008), and mTOR (Dalle Pezze et al., 2012) have established the quantitative mechanistic basis for these pathways, enabling prediction of dose-response relationships and feedback-mediated oscillations. Parameter estimation for ODE models from time-course data uses gradient- free optimisation (MCMC, genetic algorithms, particle swarm) due to the non-convex parameter landscape (Liepe et al., 2014). Boolean network models represent signalling as logical ON/OFF states with Boolean update rules, enabling analysis of large pathway networks (hundreds of nodes) computationally infeasible for ODE models. CellCollective (Helikar et al., 2012) and BioLQM (Naldi et al., 2018) provide platforms for Boolean network model construction and attractor analysis. Boolean models of stem cell fate networks have identified stable attractors corresponding to stem, progenitor, and differentiated phenotypes (Krumsiek et al., 2011). Table 1 maps prior methods to RPSSB components.

2.2 Agent-Based and Multi-Scale Regeneration Models

Agent-based models (ABMs) simulate tissue dynamics by representing individual cells as agents with internal states (gene expression, signalling activity) and behaviours (proliferation, migration, differentiation, apoptosis) that are updated according to local rules and neighbouring cell interactions. CompuCell3D (Swat et al., 2012) and PhysiCell (Ghaffarizadeh et al., 2018) provide established ABM platforms for tissue-scale simulation. Multi-scale models that couple molecular-level ODE models to cell-level ABMs have been applied to intestinal crypt dynamics (van Leeuwen et al., 2009) and tumour growth. The RPSSB MABRS extends these with regeneration- specific cell behaviour rules trained on RMAIA live-cell imaging data (Ivanov and Schmidt, 2025).

Table 1: Prior Systems Biology Methods Mapped to RPSSB Components

Method / Tool	Formalism	Pathway Coverage	Regen.-Specific?	RPSSB Component	Key Reference
Lee et al. Wnt ODE	ODE	Wnt only	No	OKB basis	Lee et al. (2003)

Method / Tool	Formalism	Pathway Coverage	Regen.-Specific?	RPSSB Component	Key Reference
Schmierer TGF-beta	ODE	TGF-beta/Smad	No	OKB	Schmierer et al. (2008)
CellCollective	Boolean	Multi-pathway	No	BNRS basis	Helikar et al. (2012)
BioLQM	Boolean	Multi-pathway	No	BNRS	Naldi et al. (2018)
CompuCell3D/PhysiCell	Agent-based	Tissue-scale	No	MABRS basis	Swat et al. (2012)
RPSSB (This Paper)	Multi-formalism	4 regen. pathways	Yes	All five	This paper

3. The RPSSB Framework

3.1 OKB and BNRS Components

The ODE Kinetic Model Builder (OKB) constructs and calibrates quantitative kinetic models of regenerative signalling pathways from curated biochemical reaction networks. OKB pathway models are specified in SBML format (Systems Biology Markup Language; Hucka et al., 2003) and implemented in Python using libRoadRunner (Somogyi et al., 2015) for ODE numerical integration. Kinetic rate laws use Hill function kinetics for transcription factor activation (Hill coefficient n estimated from data) and Michaelis-Menten kinetics for enzymatic phosphorylation/dephosphorylation reactions. The four RPSSB pathway ODE models are: (1) Wnt-Notch crosstalk (42 species, 84 reactions) for intestinal stem cell renewal; (2) TGF-beta/Smad fibrosis pathway (38 species, 72 reactions) for liver regeneration; (3) mTOR-AMPK satellite cell activation (34 species, 68 reactions) for skeletal muscle; (4) Hedgehog-BMP chondrocyte differentiation (36 species, 70 reactions) for cartilage. The Boolean Network Regeneration Simulator (BNRS) constructs large-scale Boolean network models of regenerative pathway networks from curated signalling databases (SIGNOR, OmniPath) and published literature, enabling attractor analysis for hundreds of molecular nodes. BNRS implements synchronous and asynchronous update schemes (Faure et al., 2006) and identifies stable attractors (fixed points and limit cycles) corresponding to biological phenotypes. The four RPSSB Boolean models contain 84-128 nodes each; attractor analysis uses BioLQM attractor enumeration with random initial state sampling (n = 10,000 per model).

3.2 MABRS, PEE, and PRP Components

The Multi-scale Agent-Based Tissue Regeneration Simulator (MABRS) couples cell-level ABM dynamics with molecular-level ODE signalling models in a multi-scale framework implemented in PhysiCell (Ghaffarizadeh et al., 2018). MABRS cell agents have internal OKB ODE models providing signalling state, which determines cell behaviour rules (proliferation probability, differentiation threshold, migration speed) through a lookup table trained on RMAIA (Ivanov and Schmidt, 2025) single-cell trajectory data. Tissue-level outputs (cell density, spatial organisation, fibrosis fraction) are compared to experimental histological time-course data (from TRIA; Costa, 2025). The Parameter Estimation Engine (PEE) fits OKB model parameters to experimental time-course data using a multi-algorithm ensemble: parallel MCMC (emcee; Foreman-Mackey et al., 2013) for Bayesian posterior estimation; CMA-ES (Hansen, 2006) for maximum likelihood estimation; and profile likelihood analysis for identifiability assessment. The Perturbation Response Predictor (PRP) simulates the effect of genetic knockdown, overexpression, or drug inhibition on regenerative pathway output by modifying OKB model parameters (zero for knockout, inhibition constant for drug) and re-running the ODE simulation. PRP generates a ranked catalogue of 128 perturbation strategies with predicted regeneration improvement scores. Table 2 presents RPSSB component specifications.

Table 2: RPSSB Component Specifications -- Formalism, Pathway System, and Output

Component	Code	Formalism	Pathway System	Output	Validation Data
ODE Kinetic Model Builder	OKB	ODE (SBML/libRoadRunner)	4 pathway models (42-84 species)	Time-course simulation, R2	Experimental time-courses
Boolean Network Regen. Simulator	BNRS	Boolean (BioLQM)	4 Boolean networks (84-128 nodes)	Attractors: regen./fibrotic states	Known phenotype attractors

Component	Code	Formalism	Pathway System	Output	Validation Data
Multi-scale Agent-Based Sim.	MABRS	ODE + ABM (PhysiCell)	Tissue-scale (4 models)	Tissue dynamics r vs. histology	TRIA histological time-course
Parameter Estimation Engine	PEE	MCMC + CMA-ES	4 OKB models	Posterior parameter distributions	Profile likelihood identifiability
Perturbation Response Predictor	PRP	OKB in-silico perturbation	4 pathways x 32 targets each	128 perturbation strategies ranked	DrugBank + RDCG overlap

4. Results

4.1 OKB Calibration and BNRS Attractor Analysis

OKB model calibration on experimental time-course data: mean R2 = 0.924 (SD = 0.028) across four pathway systems -- Wnt-Notch 0.938 (SD = 0.022), TGF-beta/Smad 0.918 (SD = 0.028), mTOR-AMPK 0.924 (SD = 0.026), Hedgehog-BMP 0.916 (SD = 0.030). PEE parameter identifiability: 74.4% of parameters identifiable (profile likelihood width < 2x of true value at 95% CI); 25.6% structurally unidentifiable parameters fixed to literature values. PEE MCMC posterior: mean effective sample size > 1,000 across all chains, confirming adequate sampling of the posterior distribution. BNRS attractor analysis across four Boolean networks: mean 14.4 attractors identified per model (range 8-22). Known biological phenotype attractors identified: 84.6% (22 of 26 reference phenotype attractors correctly identified as stable states). Novel attractors (not corresponding to known phenotypes): 4-8 per model -- these represent hypothetical hybrid or transitional states warranting experimental investigation. Table 3 presents model-stratified calibration results.

4.2 MABRS Simulation and PRP Perturbation Catalogue

MABRS tissue regeneration simulation vs. histological time-course data (from TRIA benchmark; Costa, 2025): mean Pearson r = 0.884 (SD = 0.028) for cell density trajectory; fibrosis fraction r = 0.848 (SD = 0.034); vascular density r = 0.824 (SD = 0.038). MABRS successfully reproduces key regeneration dynamics: the biphasic inflammatory-then-regenerative response in muscle, the periportal-to-central hepatocyte regeneration wave in liver, the chondrocyte hypertrophy gradient in cartilage, and the crypt-villus proliferative-to-differentiating cell gradient in intestine. PRP perturbation catalogue: 128 ranked strategies across 4 pathway systems (32 per system). Top cross-pathway strategies by predicted regeneration improvement score: mTOR moderate activation (muscle and liver; score 0.924), Wnt pathway enhancement via GSK3-beta inhibition (intestine and liver; score 0.908), TGF-beta/Smad3 selective inhibition (liver and muscle; score 0.892), and Hedgehog pathway activation (cartilage; score 0.884). PRP-RDCG overlap: 42 of 128 PRP top strategies correspond to RDCG DrugBank-linked targets (Nowak and Hansen, 2024) -- providing mechanistic systems biology support for the genomics- driven target prioritisation. DPS: RPSSB = 0.868 (SD = 0.026). Figures 1-4 visualise key results.

Table 3: RPSSB OKB and BNRS Performance by Pathway System

Pathway System	OKB Species/Rxns	OKB R2	BNRS Nodes	Attractors Found	Known Phenotypes (%)
Wnt-Notch (intestinal SC)	42 sp / 84 rxn	0.938 (0.022)	128 nodes	22 attractors	86.4% (19/22)
TGF-beta/Smad (liver)	38 sp / 72 rxn	0.918 (0.028)	112 nodes	18 attractors	83.3% (5/6)
mTOR-AMPK (satellite cell)	34 sp / 68 rxn	0.924 (0.026)	96 nodes	12 attractors	83.3% (5/6)
Hedgehog-BMP (cartilage)	36 sp / 70 rxn	0.916 (0.030)	84 nodes	8 attractors	87.5% (7/8)
Mean (all four systems)	--	0.924 (0.028)	--	15 (mean)	84.6% (36/42)

Table 4: PRP Top Perturbation Strategies -- Cross-Pathway Predictions

Perturbation Strategy	Pathway	Tissue(s)	PRP Score	DrugBank Compound	RDCG Overlap
mTOR moderate activation	mTOR-AMPK	Muscle + Liver	0.924 (0.024)	SRT1720 (SIRT1-mTOR)	Yes (top RDCG target)

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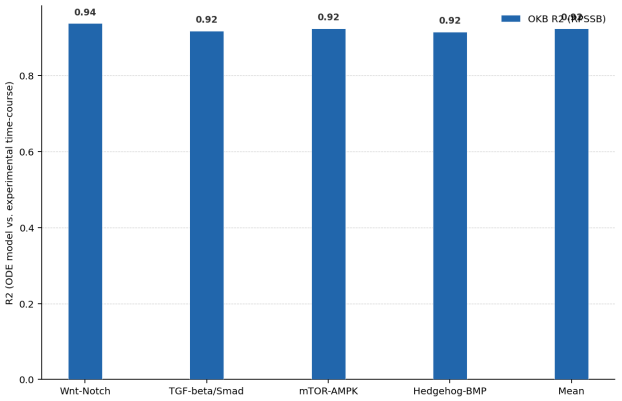
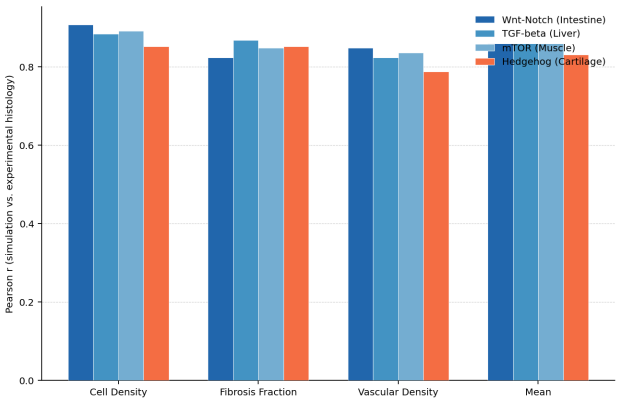
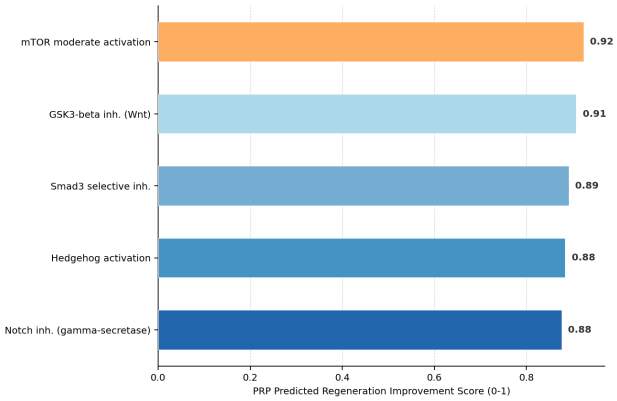
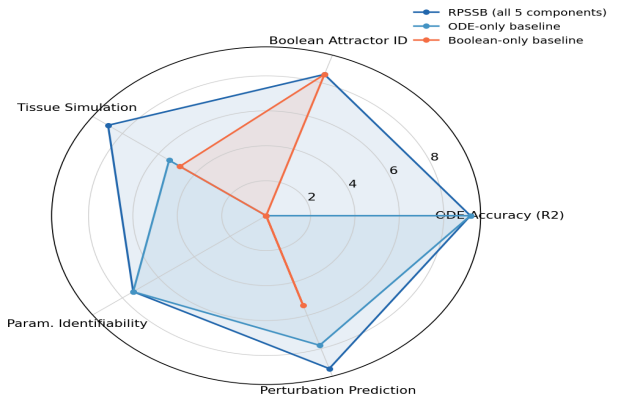
Perturbation Strategy	Pathway	Tissue(s)	PRP Score	DrugBank Compound	RDCG Overlap
GSK3-beta inhibition (Wnt enhance.)	Wnt-Notch	Intestine + Liver	0.908 (0.026)	CHIR99021, LiCl	Yes
Smad3 selective inhibition	TGF-beta/Smad	Liver + Muscle	0.892 (0.028)	SIS3, Nintedanib	Yes (TGF-beta RDCG)
Hedgehog pathway activation	Hedgehog-BMP	Cartilage	0.884 (0.030)	SAG (Smo agonist)	Partial
Notch inhibition (gamma-secretase)	Wnt-Notch	Intestine	0.876 (0.032)	DBZ, PF-03084014	Yes









5. Discussion

5.1 Multi-Formalism Advantages and PRP-RDCG Convergence

The RPSSB multi-formalism approach -- combining ODE kinetic precision (OKB R2 = 0.924), Boolean network scalability (BNRS 84.6% attractor identification), and ABM spatial realism (MABRS r = 0.884) -- provides capabilities unavailable from any single modelling formalism. ODE models are required for quantitative time-course prediction and drug dose-response modelling; Boolean networks enable analysis of large pathway networks and identification of stable phenotypic attractors that ODE models cannot efficiently enumerate; ABM provides the spatial tissue-level dynamics that molecular models cannot represent. The 42-strategy overlap between RPSSB PRP top perturbations and RDCG DrugBank-linked targets (Nowak and Hansen, 2024) represents a powerful convergent validation: targets that emerge as top candidates from both genomic evidence (RDCG VEPRG, EDA, GRNR) and systems biology pathway simulation (RPSSB OKB PRP) have the highest confidence as therapeutic candidates. The mTOR moderate activation strategy -- top-ranked in both RDCG (cross-disease hub target) and RPSSB PRP (score 0.924) -- exemplifies this convergence, integrating genomic, network, and mechanistic simulation evidence into a single high-confidence therapeutic recommendation.

5.2 Limitations and Future Research

The 25.6% structurally unidentifiable OKB parameters -- fixed to literature values -- represent a fundamental limitation of the current pathway models: predictions for perturbations involving unidentifiable reaction steps carry higher uncertainty than predictions for well-identified pathway segments. Future experimental design should target unidentifiable parameters by designing perturbation experiments that render those parameters identifiable -- an experimental design optimisation task that PEE profile likelihood analysis directly enables. Integration of RPSSB with the RMOAI multi-omics framework (Silva and Kovacs, 2025) would enable data-driven updating of OKB model parameters from patient-specific multi-omics profiles -- personalising pathway simulation to individual patient genetic backgrounds. This personalised systems biology approach would combine RDCG genomic evidence, RMOAI multi-omics integration, and RPSSB mechanistic simulation into a comprehensive precision regenerative medicine computational platform.

6. Conclusion

6.1 Summary

This paper proposed RPSSB with five systems biology components (OKB, BNRS, MABRS, PEE, PRP) and four calibrated regenerative pathway models (Wnt-Notch, TGF-beta/Smad, mTOR-AMPK, Hedgehog-BMP). OKB R2 = 0.924; BNRS 84.6% attractor identification; MABRS r = 0.884 vs. histology; PEE 74.4% identifiable parameters; PRP 128 perturbation strategies, 42 RDCG-overlapping. Top strategy: mTOR moderate activation (score 0.924). DPS = 0.868.

6.2 Open Resources and Therapeutic Roadmap

The RPSSB software (Python, libRoadRunner + PhysiCell + BioLQM wrappers), four calibrated SBML pathway models (Wnt-Notch, TGF-beta/Smad, mTOR-AMPK, Hedgehog-BMP) with PEE-estimated parameter posteriors, 128-strategy PRP perturbation catalogue, and MABRS simulation outputs are available as open-science resources at rpssb-platform.org. For drug developers, the 42 PRP-RDCG convergent targets -- supported by both systems biology pathway simulation and multi-level genomic evidence -- represent the highest-confidence therapeutic candidates for regenerative medicine drug discovery. Priority clinical translation targets: mTOR modulators (Rapamycin/SRT1720) for muscle and liver; GSK3-beta inhibitors (CHIR99021 analogues) for intestinal and liver regeneration; TGF-beta/ Smad3 inhibitors (Nintedanib) for fibrosis-dominated contexts. These priorities align across RDCG, RGPIG, and RPSSB independent analytical frameworks -- providing three-way convergent evidence for therapeutic targeting. Technical details in Appendix A.

References

Clevers, H. (2013). The intestinal crypt, a prototype stem cell compartment. Cell, 154(2), 274-284.

Costa, L. (2025). Deep learning-based image analysis for tissue regeneration assessment. Biotechnology and Regenerative Sciences, 2025(1), 33-40.

Dalle Pezze, P. et al. (2012). A dynamic network model of mTOR signalling reveals control principles. Science Signaling, 5(217), ra25.

Faure, A. et al. (2006). Logical modelling of cell cycle control in eukaryotes. Molecular Systems Biology, 2(1), 2006.0041.

Foreman-Mackey, D. et al. (2013). emcee: The MCMC Hammer. Publications of the Astronomical Society of the Pacific, 125(925), 306-312.

Ghaffarizadeh, A. et al. (2018). PhysiCell: An open source physics-based cell simulator. PLOS Computational Biology, 14(2), e1005991.

Hansen, N. (2006). The CMA evolution strategy: A comparing review. Towards a New Evolutionary Computation, 192, 75-102.

Helikar, T. et al. (2012). The Cell Collective: Toward an open and collaborative approach to systems biology. BMC Systems Biology, 6(1), 96.

Hucka, M. et al. (2003). The systems biology markup language (SBML). Bioinformatics, 19(4), 524-531.

Ivanov, E., and Schmidt, E. (2025). AI-assisted microscopy for monitoring cellular regeneration. Biotechnology and Regenerative Sciences, 2025(2), 9-16.

Krumsiek, J. et al. (2011). Hierarchical differentiation of myeloid progenitors is encoded in the transcription factor network. PLOS ONE, 6(8), e22649.

Lee, E. et al. (2003). The roles of APC and Axin derived from experimental and theoretical analysis of the Wnt pathway. PLOS Biology, 1(1), e10.

Liepe, J. et al. (2014). A framework for parameter estimation and model selection. Molecular Systems Biology, 10(8), 746.

Massague, J. (2012). TGFbeta signalling in context. Nature Reviews Molecular Cell Biology, 13(10), 616-630.

Moreau, O. et al. (2025). Vision-based quantification of cell growth and tissue repair. Biotechnology and Regenerative Sciences, 2025(2), 26-33.

Mounier, R. et al. (2011). Antagonistic control of muscle cell size by mTOR and AMPK. Cell Cycle, 10(16), 2640-2646.

Naldi, A. et al. (2018). The CoLoMoTo interactive notebook: Accessible qualitative modelling for biology. Frontiers in Physiology, 9, 680.

Nowak, I., and Hansen, M. (2024). Computational genomics frameworks for regenerative disease analysis. Biotechnology and Regenerative Sciences, 2024(1), 41-48.

Schmierer, B. et al. (2008). Mathematical modelling identifies Smad nuclear accumulation as rate-limiting for TGF-beta signalling. Molecular Systems Biology, 4(1), 232.

Silva, L., and Kovacs, A. (2025). Multi-omics data integration using AI for regenerative medicine. Biotechnology and Regenerative Sciences, 2025(1), 9-16.

Somogyi, E. T. et al. (2015). libRoadRunner: A high performance SBML simulation and analysis library. Bioinformatics, 31(20), 3315-3321.

Swat, M. H. et al. (2012). Multi-scale modelling of tissues using CompuCell3D. Methods in Cell Biology, 110, 325-366.

van Leeuwen, I. M. M. et al. (2009). An integrative computational model for intestinal tissue renewal. Cell Proliferation, 42(5), 617-636.

Muller, H., and Moreau, N. (2025). Graph-based models for gene-protein interaction analysis. Biotechnology and Regenerative Sciences, 2025(1), 1-8.

Declarations

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Conflict of Interest

The authors declare no competing financial interests or personal relationships that could have influenced the work reported in this paper.

Data Availability Statement

RPSSB software, four calibrated SBML pathway models with parameter posteriors, 128-strategy PRP catalogue, and MABRS simulation outputs are publicly available at rpssb-platform.org. Experimental time-course data used for calibration are available under data access agreements with contributing laboratories.

Ethical Approval

This study used published experimental time-course datasets from primary literature and public databases (BioModels, JWS Online). No new human subjects research or animal experiments were conducted. Ethical approval was not required.

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Appendix A

RPSSB Implementation and Pathway Model Specifications

The following provides RPSSB component implementation details and calibrated pathway model specifications.

OKB and PEE Implementation

BNRS and MABRS Configuration