

# Control Methods for Dynamic Cellular Simulations of Fibrosis



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BACKGROUND: Predicting control strategies for Agent-Based Models (ABMs) is often slow and computationally expensive. We hypothesize that integrating machine learning with ABM can significantly reduce simulation time while yielding interpretable results and effective control strategies for complex systems. To test this hypothesis, we applied our approach to a pulmonary fibrosis model.

## Methods

Data Collection

Agent-Based Model

ODE-based Signaling

Interpretable Analysis

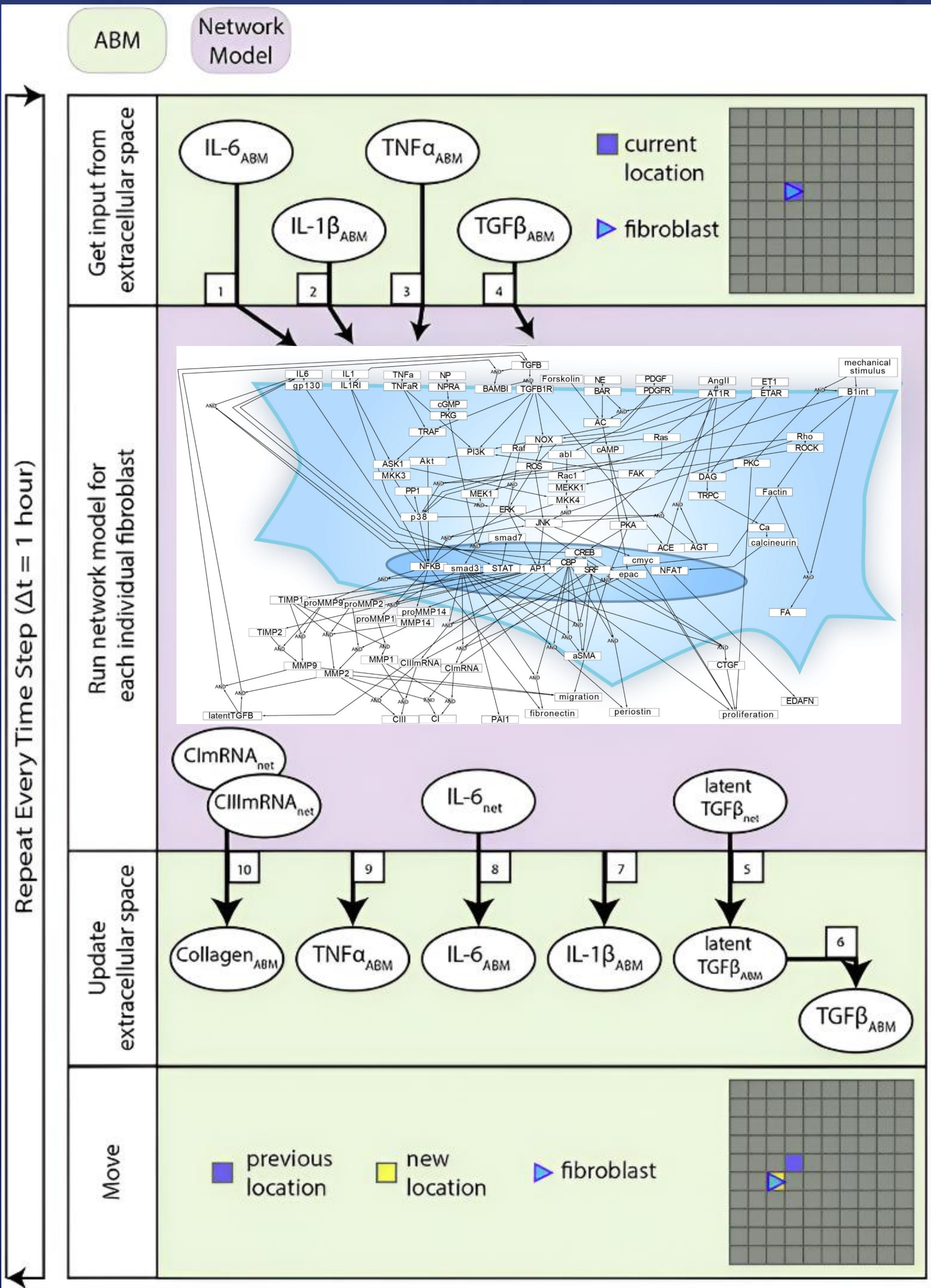
Random Forrest

Sobol Sensitivity Analysis

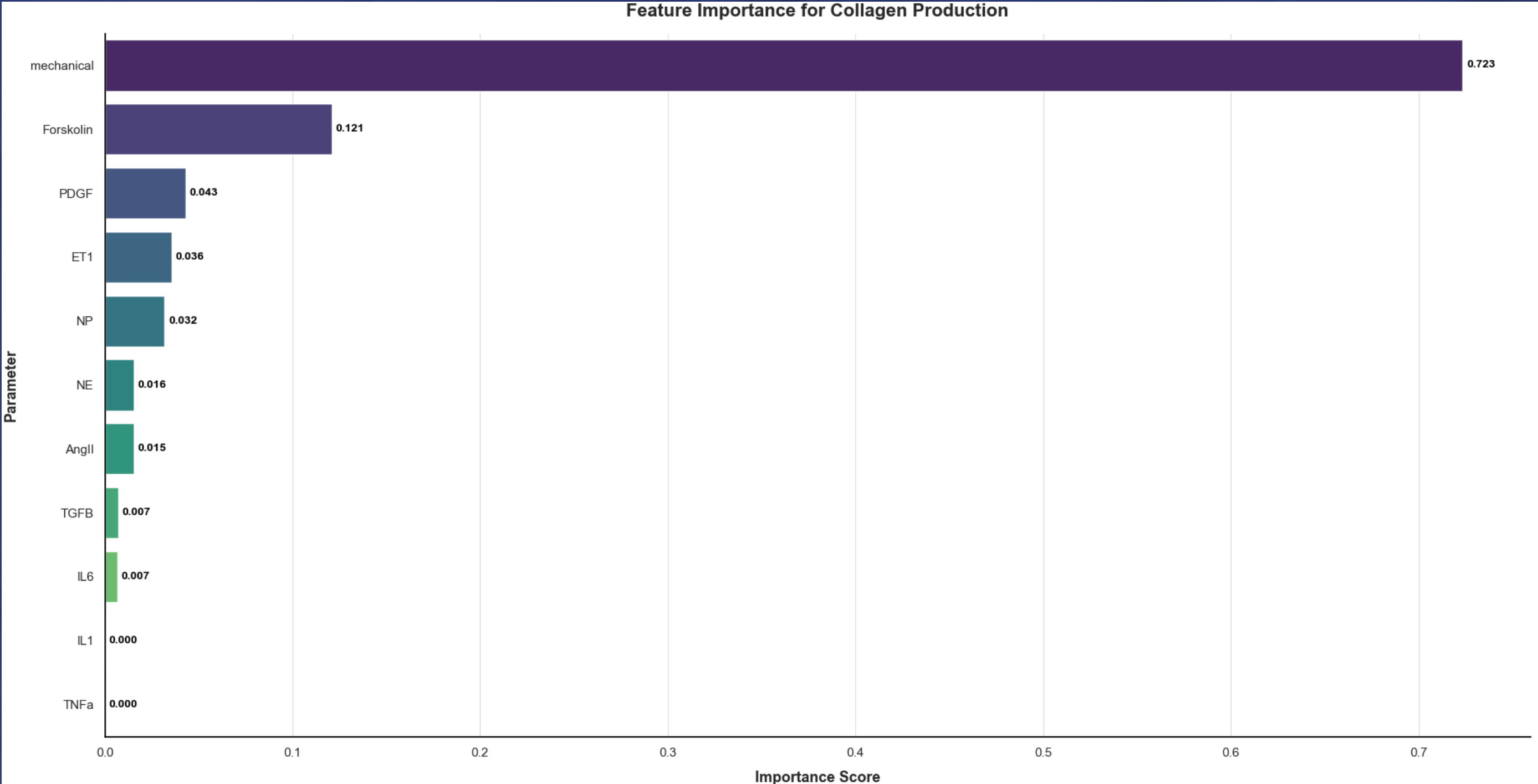
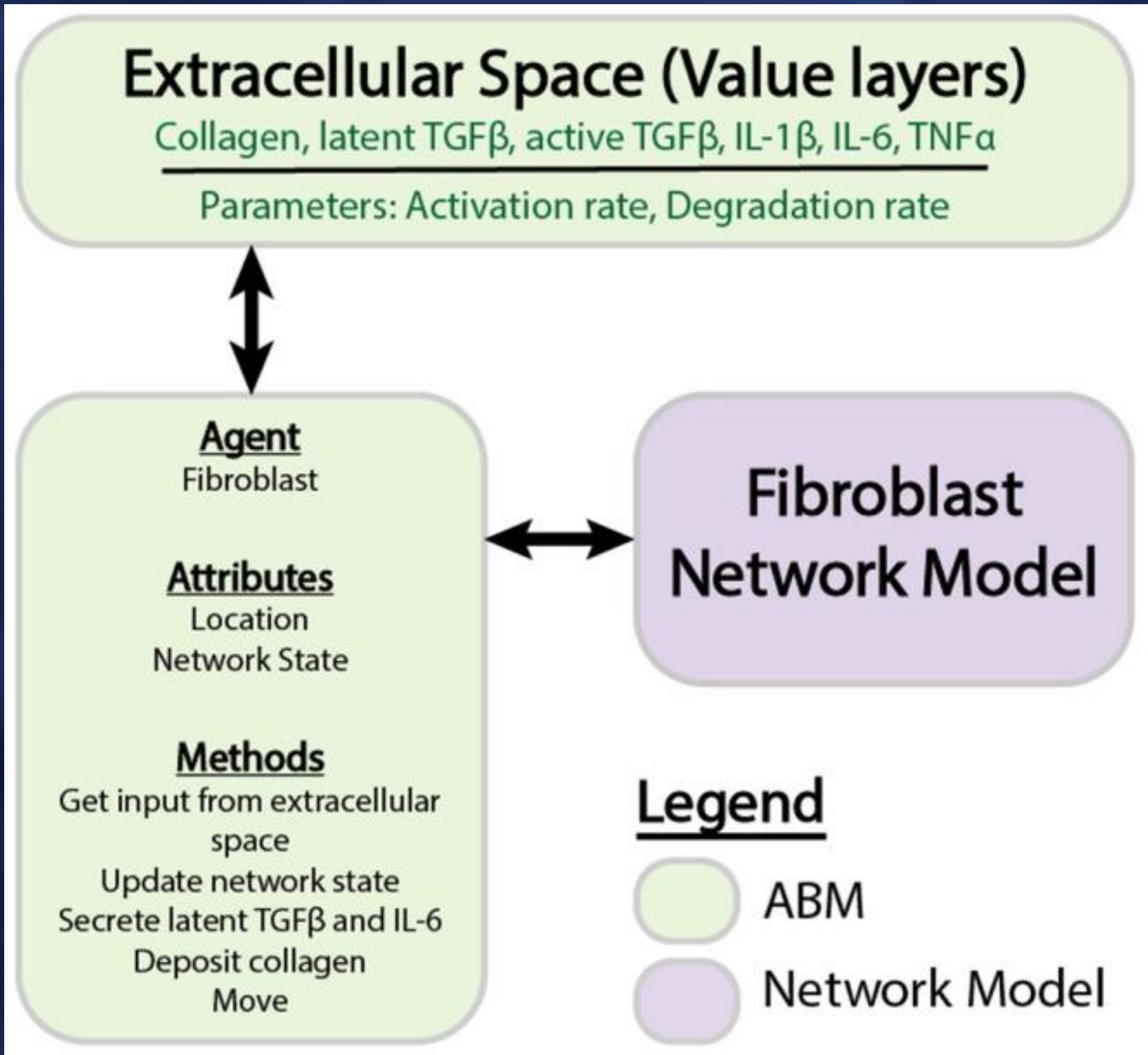
SHAP (SHapley Additive  
exPlanations)

Monte Carlo Simulations

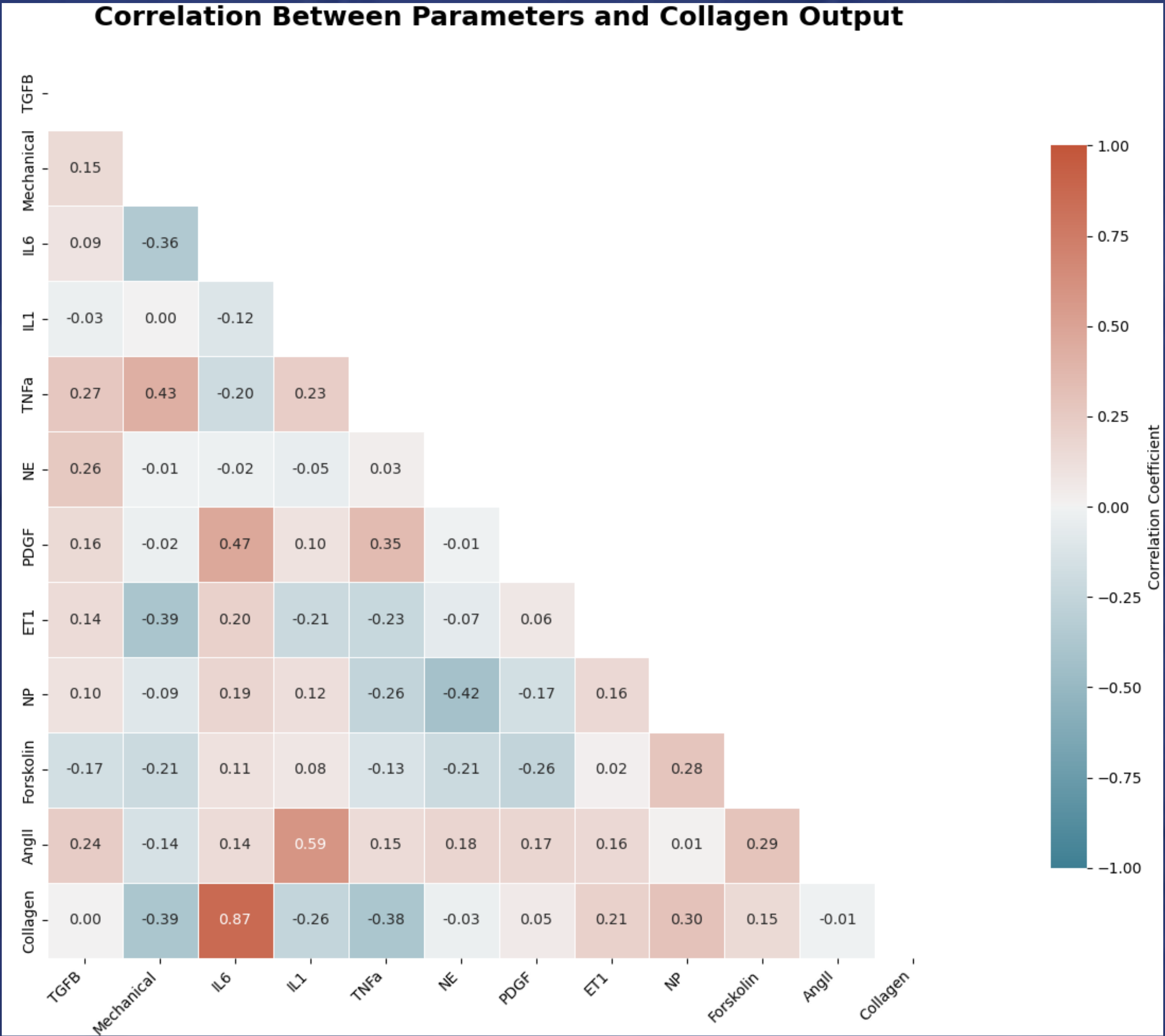
Effective control strategies boost speed, cut costs, and streamline analysis of complex model simulations.



Illustrating the correlation of ODE and ABM in Fibrosis Modeling



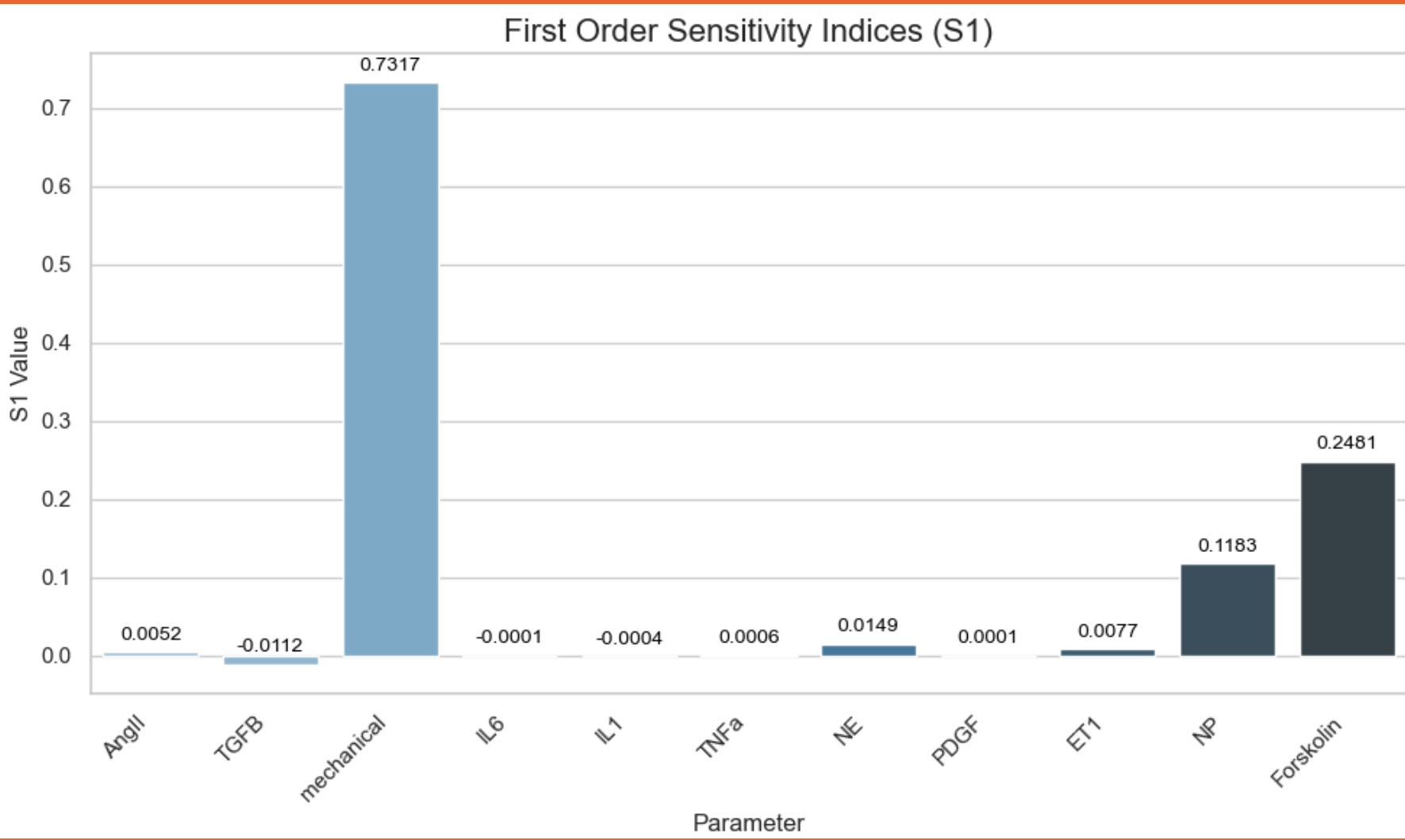
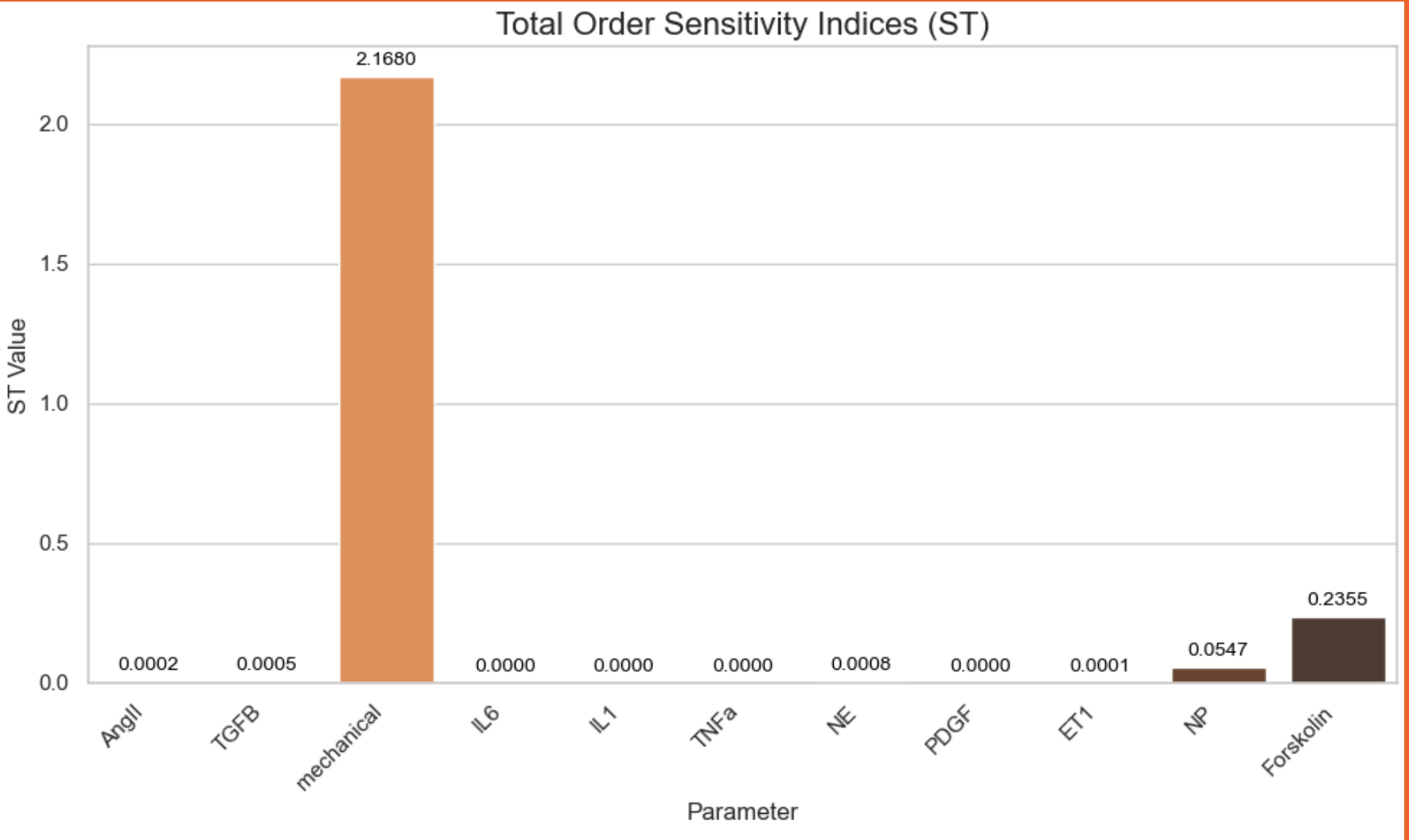
Random Forrest Feature Importance for Collagen Production



Monte Carlo Parameter Correlation to Collagen



## Results



## Discussion

**Efficient Analysis:** Blends machine learning and math to simplify complex biological simulations, spotlighting key fibrosis drivers like TGFβ and IL-6.

**Insightful Tools:** Random Forest, Sobol, SHAP, and Monte Carlo pinpoint critical factors and interactions with minimal simulations.

**Big Potential:** Scalable framework for fibrosis therapies and beyond, from oncology to immunology.

## References

Rikard, S. M., Athey, T. L., Nelson, A. R., Saucerman, J. J., & et al. (2019). Multiscale coupling of an agent-based model of tissue fibrosis and a logic-based model of intracellular signaling. *Frontiers in Physiology*, 10, 1481. <https://doi.org/10.3389/fphys.2019.01481>

Zeigler, A. C., Richardson, W. J., Holmes, J. W., & Saucerman, J. J. (2016). A computational model of cardiac fibroblast signaling predicts context-dependent drivers of myofibroblast differentiation. *Journal of Molecular and Cellular Cardiology*, 94, 72-81. <https://doi.org/10.1016/j.yjmcc.2016.03.008>

**Acknowledgements**  
Dr. Luis Sordo Vieira