

Dear Guest Editors,

We are pleased to submit our manuscript entitled “**Experimenting with Reaction Systems using Graph Transformation and GROOVE**” and authored by Roberto Bruni and myself for consideration in the upcoming special issue of *Natural Computing*, following the 2024 workshop on Reaction Systems held in Pisa.

Our contribution explores the capabilities of GROOVE, a state-of-the-art toolset based on graph transformation systems, to analyze Reaction Systems through reachability analysis, causal analysis, and model checking. Our work highlights how Reaction Systems can be naturally and efficiently encoded within GROOVE, leading to encouraging results. Notably, we show that GROOVE can drastically reduce the analysis time in handling large state spaces for key tasks such as reachability and causal exploration w.r.t. existing tools.

The manuscript also provides insights from the perspective of graph transformation, including how GROOVE’s versatile support for nested and negative application conditions aids in modeling Reaction Systems semantics and how the conducted experimentation provided some feedback to enhance GROOVE with new functionalities and to improve its usability. We believe that our study can be of some interest to both researchers in formal methods and practitioners working with computational models of biological systems.

This manuscript is an original submission and is not under consideration for publication elsewhere.

Thank you very much for the opportunity to contribute to this special issue.

We look forward to your feedback.

Sincerely,

Arend Rensink

(on behalf of both authors)