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Applications Note

Systems biology

# SpaceScanner: COPASI wrapper for automated management of global stochastic optimization experiments

**Atis Elsts,[1] Agris Pentjuss[2] and Egils Stalidzans[2,]***

[1]Department of Electrical and Electronic Engineering, University of Bristol, Bristol BS8 1UB, UK and [2]Institute of Microbiology and Biotechnology, University of Latvia, Riga LV-1004, Latvia

*To whom correspondence should be addressed.
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## Abstract

**Motivation:** Due to their universal applicability, global stochastic optimization methods are popular for designing improvements of biochemical networks. The drawbacks of global stochastic optimization methods are: (i) no guarantee of finding global optima, (ii) no clear optimization run termination criteria and (iii) no criteria to detect stagnation of an optimization run. The impact of these drawbacks can be partly compensated by manual work that becomes inefficient when the solution space is large due to combinatorial explosion of adjustable parameters or for other reasons.
**Results:** SpaceScanner uses parallel optimization runs for automatic termination of optimization tasks in case of consensus and consecutively applies a pre-defined set of global stochastic optimization methods in case of stagnation in the currently used method. Automatic scan of adjustable parameter combination subsets for best objective function values is possible with a summary file of ranked solutions.
**Availability and implementation:** https://github.com/atiselsts/spacescanner.
**Contact:** egils.stalidzans@lu.lv
**Supplementary information:** Supplementary data are available at *Bioinformatics* online.

## 1 Introduction

Global stochastic optimization methods that are implemented in COPASI software tool (Hoops *et al.*, 2006) are popular due to their applicability independent of the nonlinearity of the model. Another important feature is easily switching between global stochastic methods as no transformation of the original problem is needed (Moles *et al.*, 2003). At the same time, their application may lead to incorrect conclusions in the case of inappropriate optimization duration, optimization method or its settings. The performance of a global stochastic optimization method also depends on the type of problem (Balsa-Canto *et al.*, 2012) and testing several methods for the same task is important. Parallel optimization runs have been applied to address the drawbacks of global stochastic optimization methods by studying their convergence (Kostromins *et al.*, 2012), convergence and stagnation criteria (Mozga and Stalidzans, 2011), automatic detection of stagnation and consensus (Sulins and Mednis, 2012). SpaceScanner (abbreviated from 'adjustable parameter solution **space scanner**') is a handy optimization automation and analysis oriented COPASI wrapper with graphical user interface for systems biology specialists without programing background. It supports: (i) parallel optimization runs with automated recognition of consensus and stagnation situations, (ii) automatic switching between different user-selected global stochastic optimization methods in case of stagnation in the current method, (iii) determination of the best sets of adjustable parameters (Stalidzans *et al.*, 2016) for a pre-set range of a number of adjustable parameters in combination and (iv) search for the minimal number of adjustable parameters that can reach the requested fraction of the total optimization potential (TOP approach; Stalidzans *et al.*, 2016). Parallel optimization runs can be initiated using the COPASI wrapper Condor-COPASI

 

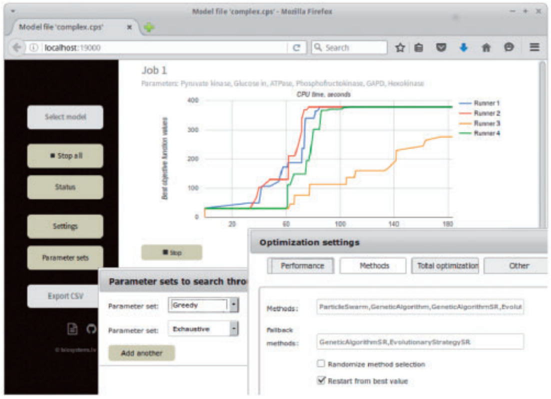


**Fig. 1.** The web interface of *SpaceScanner*. Visible: optimization history for a subset of adjustable parameters (main pane, background), parameter set selection dialogue (main pane, bottom left), and optimization settings dialogue (main pane, bottom right), the main command menu (sidebar)

(Kent *et al.*, 2012) while the rest of SpaceScanner functionality is not supported. Furthermore SpaceScanner differs as it (i) can be run locally on the user's PC since it does not require a complex installation, (ii) guarantees real-time simultaneity of parallel optimizations via CPU core load-balancing and (iii) graphs the results in real-time, allowing for better interactivity.

## 2 Implementation and features

The kinetic model file of interest has to be in COPASI format (.cps) (Hoops *et al.*, 2006) and set up for execution of optimization task: must include an objective function (optimization criterion) and a list of adjustable parameters with a permitted range of values (Supplementary Material S1). Internally, SpaceScanner uses COPASI to execute the optimizations.

SpaceScanner helps to automate execution of multiple parallel optimization runs by starting multiple identical COPASI optimizations (they differ during execution because of the stochastic component). The tool is capable of automatic termination when the runs have reached nearly identical (consensus) values (Sulins and Mednis, 2012), and automated change of the optimization method in case of stagnation (Sulins and Mednis, 2012). The user is able to observe the history of optimization runs in dynamically updated graphs (Fig. 1).

SpaceScanner can be configured to automatically analyse the space of all or user defined subsets from the set of adjustable parameter combinations. This is useful for more advanced automation tasks, e.g. to rank the subsets according to their objective function value. This is handy when a limited number of parameters from the adjustable parameter set can be improved during strain engineering (e.g. because of biological constraints or economical limitations). Another application of this functionality is to determine the minimal subset of parameters that gives 'good enough' results according user-defined rules, e.g. that gives 90% of TOP (Stalidzans *et al.*, 2016).

SpaceScanner outputs the following per optimization task:

- a .csv file with optimization results, with a row for each parameter subset evaluated;
- a .log file with SpaceScanner execution history.

SpaceScanner outputs the following for each optimized set of parameters:

- a .txt file for each optimization run with COPASI optimization history;
- a .cps COPASI file for each optimization run with the parameters set to their best (final) values.

SpaceScanner at the moment supports a greedy and exhaustive (brute-force) search of all adjustable parameter subsets. More advanced search strategies (e.g. global stochastic search, parameter sensitivity-informed search, MFA-informed search) are planned as future additions.

SpaceScanner is implemented in Python and works on all major operating systems, is easy to use and configure, and features two interfaces:

- a command-line interface that expects a configuration file in JSON format as the only argument;
- a platform-independent web interface that allows the user to interactively configure, start, and stop optimization runs, as well as see their results graphically (Fig. 1).

## 3 Discussion

The automation of optimization by global stochastic methods and automated representation of results are the main SpaceScanner features that are very important when many combinations of parameters are being analysed (solution space scanning) and/or in case of a model with unknown optimization convergence speed.

Automatic termination of optimization runs in combination with change of optimization methods in case of stagnation enables automatic analysis of a minimal set of adjustable parameters to reach a pre-defined fraction of TOP (Stalidzans *et al.*, 2016) (case study in Supplementary Material S2) generating a ranked summary file with thousands of analysed combinations.

SpaceScanner can have more conservative settings: (i) increasing number of parallel runs, (ii) reducing consensus corridor and (iii) increasing delay time settings. Thus, if high confidence about reaching global optima is needed (still with no guarantee), conservative consensus criteria may be used requiring increased time and computational costs of optimization. When looking for a fast scan of solution space to find, for instance, the minimal set of parameters (Stalidzans *et al.*, 2016), the settings may be more relaxed (case study in Supplementary Material S3).

*Conflict of Interest*: none declared.

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