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Subject Section

SpaceScanner: COPASI wrapper for automated management of global stochastic optimisation experiments

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Abstract

Motivation: Due to their universal applicability, global stochastic optimisation methods are popular for designing improvements of biochemical networks. The drawbacks of global stochastic optimisation methods are: 1) no guarantee of finding global optima, 2) no clear optimisation run termination criteria and 3) no criteria to detect stagnation of an optimisation 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 optimisation runs for automatic termination of optimisation tasks in case of consensus and consecutively applies a pre-defined set of global stochastic optimisation 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

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Supplementary information: Supplementary data are available at *Bioinformatics* online.

1 Introduction

Global stochastic optimisation 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 optimisation duration, optimisation method or its settings. The performance of a global stochastic optimisation method also depends on the type of problem (Balsa-Canto et al., 2012) and testing several methods for the same task is important. Parallel optimisation runs have been applied to handle the drawbacks of global stochastic optimisation methods 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 optimisation automation and analysis oriented wrapper with graphical user interface for systems biology specialists without programing background. It supports: 1) parallel optimisation runs with automated recognition of consensus and stagnation situations, 2) automatic switching between different user-selected global stochastic optimisation methods in case of stagnation in the current method, 3) 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 4) search for the minimal number of adjustable parameters that can reach the requested fraction of the total optimisation potential (TOP approach (Stalidzans et al., 2016)). Parallel optimisation runs can be initiated on a COPASI wrapper Condor-COPASI (Kent *et al.*, 2012) while the rest of SpaceScanner functionality is not supported. Furthermore SpaceScanner differs as it (1) can be run locally on the user's PC since it does not require a complex installation, (2) guarantees real-time simultaneity of parallel optimisations via CPU core load-balancing, and (3) 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 optimisation task: must include an objective function (optimisation criterion) and a list of adjustable parameters with a permitted range of values (Suppl. mat. 1). Internally, SpaceScanner uses COPASI to execute the optimisations.

SpaceScanner helps to automate execution of multiple parallel optimisation runs starting with multiple identical COPASI optimisations (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 optimisation method in case of stagnation (Sulins and Mednis, 2012). The user is able to observe the history of optimisation runs in dynamically updated graphs (Figure 1).
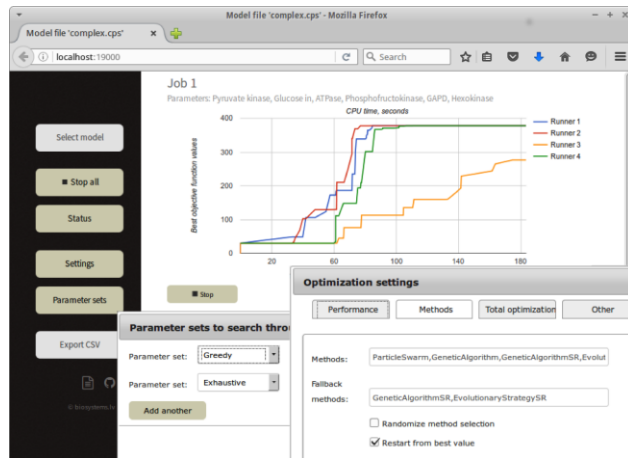
Figure 1. The web interface of *SpaceScanner*. Visible: optimisation history for a subset of adjustable parameters (main pane, background), parameter set selection dialog (main pane, bottom left), and optimisation settings dialog (main pane, bottom right), the main command menu (sidebar).

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 optimisation task:
*   a .csv file with optimisation results, with a row for each parameter subset evaluated;
*   a .log file with SpaceScanner execution history.

SpaceScanner outputs the following for each optimised set of parameters:
*   a .txt file for each optimisation run with COPASI optimisation history;
*   a .cps COPASI file for each optimisation 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 optimisation runs, as well as see their results graphically (Figure 1).

3   Discussion

The automation of optimisation 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 optimisation convergence speed.

Automatic termination of optimisation runs in combination with change of optimisation 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 Suppl. mat. 2) generating a ranked summary file with thousands of analysed combinations.

SpaceScanner can have more conservative settings: 1) increasing number of parallel runs, 2) reducing consensus corridor and 3) 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 optimisation. 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 Suppl. mat. 3).

Conflict of Interest: none declared.

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