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***webLSA: integrated local similarity analysis and network visualization of biological series data***

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***Keywords:*** Local Similarity Analysis, Time Series Data, Network Visualization

*Background*

Identifying ecological and biochemical associations in time, spatial and other series of biomolecules from genome, transcriptome and proteome is routinely required in current bioinformatics. Analyzing these co-occurrence and co-expression patterns are fundamental to reveal the underlying biological relations **(1,2)**. Among the computational methods developed for such tasks, Local Similarity Analysis (**LSA**) has gained significant audience, for its unique ability to captures local and potentially time-delayed (or space-shifted) associations that cannot otherwise be identified with ordinary correlation analysis **(3)**.

LSA has been actively developed **(4-7)**, vigorously validated **(2)**, independently top benchmarked **(3)**, and widely applied with high impacts **(1,8-16)**. Its milestone papers **(1,4-7,17)** received more than 1200 citations to date. A Python package (eLSA) **(4)** is freely available for practitioners to conduct LSA, yet feature requests for web-based workflow and integrated network visualization were consistently received. As a response, we present webLSA, an integrated local similarity analysis and network visualization service dedicated to biological series data, with the hope to make LSA more accessible to a wider community.

*Methods*

The backend of webLSA is based on the same Local Similarity Analysis algorithm that has been developed, improved, and extensively validated since 2006 **(4-7)**. The statistical significance estimation in webLSA employed the approximation theory developed in 2013 **(6)**. webLSA made many improvements including: a) multi-threading acceleration in the backend taking advantage of multi-core CPUs; b) leveraging the Galaxy server **(18)** for frontend, enabling community-tested and user-friendly data and workflow management; and c) achieving on-the-fly and interactive massive network visualization using the state-of-art Graphistry APIs **(19)**.

*Input/Output*

webLSA accepts a user uploaded plain txt table containing possibly replicated series data. It also requires the user to submit a set of parameters on the run request form. The front and back ends of webLSA are decoupled so that a user can submit multiple jobs meanwhile monitor the status. The output is a plain txt table containing the local associations and their statistics, p-values, false discovery rates, and other relevant information. The inputs and outputs follow the specification of the widely used eLSA tool, and are explained in the numerous hints, helps and demos available on the webserver. The output is visualizable on webLSA as an interactive network, for intuitive exploration, pruning, annotation and export to standard graph file formats.

*Applications*

We had a demo page on webLSA tutoring the LSA of a marine microbiome series consisting of 72-hour bi-hourly data of thousands of amplicon sequence variants, with detailed discussions of the identified associations and their ecological implications.

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***Cover Letter***

Dear Editor,

We are submitting webLSA for consideration for the upcoming NAR webserver issue.

Identifying ecological and biochemical associations in time and other series data from genome, transcriptome and proteome is routinely required in current bioinformatics. Analyzing these co-occurrence patterns are fundamental to reveal the underlying relations. Among the computational methods for such tasks, Local Similarity Analysis (**LSA**) has gained significant audience, for its unique ability to captures local and potentially time-delayed (or space-shifted) associations that cannot otherwise be identified with ordinary correlation analysis [1].

LSA has been actively developed, vigorously validated, independently top benchmarked [2], and widely applied with high impacts [1]. Its methodological papers received more than 700 citations to date. A Python package (eLSA) is freely available for practitioners to conduct LSA, while feature requests for web-based workflow and integrated network visualization were consistently received. As a response, we present webLSA, an integrated local similarity analysis and network visualization service dedicated to biological series data, with the hope to make LSA more accessible to a wider community. Thank you for consideration.

Li C. Xia

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***Summary***

***Methods*:** The backend of webLSA is based on the same Local Similarity Analysis algorithm that has been developed, improved, and extensively validated since 2006 [3,4]. The statistical significance estimation in webLSA employed the approximation theory developed in 2013 [5]. Improvements of webLSA include: multi-threading acceleration taking advantage of multi-core CPUs; leveraging the Galaxy server [6]to enable user-friendly data and workflow management; and achieving on-the-fly interactive massive network visualization using the state-of-art Graphistry APIs[7].

***Input/Output:*** webLSA accepts a user uploaded table containing possibly replicated series data. It also requires the user to submit a set of parameters on the run request form. The front and back ends of webLSA are decoupled so that a user can submit multiple jobs meanwhile monitor the status. The output is a table containing the local associations and their statistics, p-values, false discovery rates, and other relevant information. The inputs and outputs follow the specification of the widely used eLSA tool, and are explained in the numerous hints, helps and demos available on the webserver. The output is visualizable on webLSA as an interactive network, for intuitive exploration, pruning, annotation and export to standard graph file formats.

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[6] Galaxy: https://github.com/galaxyproject/galaxy.

[7] Graphistry: https://github.com/graphistry/pygraphistry.