Systems biology

PyIOmica: longitudinal omics analysis and trend identification

Sergii Domanskyi1, Carlo Piermarocchi1 and George I. Mias 1,2,3,*

1Department of Physics and Astronomy, 2Department of Biochemistry and Molecular Biology and 3Institute for Quantitative Health Science and Engineering, Michigan State University, East Lansing, MI 48824, USA

*To whom correspondence should be addressed.

Received on July 19, 2019; revised on October 26, 2019; editorial decision on November 23, 2019; accepted on November 26, 2019

Abstract

Summary: PyIOmica is an open-source Python package focusing on integrating longitudinal multiple omics datasets, characterizing and categorizing temporal trends. The package includes multiple bioinformatics tools including data normalization, annotation, categorization, visualization and enrichment analysis for gene ontology terms and pathways. Additionally, the package includes an implementation of visibility graphs to visualize time series as networks.

Availability and implementation: PyIOmica is implemented as a Python package (pyiomica), available for download and installation through the Python Package Index (https://pypi.python.org/pypi/pyiomica), and can be deployed using the Python import function following installation. PyIOmica has been tested on Mac OS X, Unix/Linux and Microsoft Windows. The application is distributed under an MIT license. Source code for each release is also available for download on Zenodo (https://doi.org/10.5281/zenodo.3548040).

Contact: gmias@msu.edu

Supplementary information: Supplementary data are available at Bioinformatics

1 Introduction

As sequencing costs continue to drop, systems biology based on large omics datasets is rapidly expanding its scope. In particular, time series obtained from multi-omics datasets are becoming more and more affordable (Chen et al., 2012; Garrett-Bakelman et al., 2019; Price et al., 2017). The analysis of time series can have broad implications for precision medicine applications, since longitudinal data capture the dynamically changing collective microscopic behavior of molecular components in the body, reflecting the physiologic state of a patient. There are many bioinformatics tools aiming at multimodal omics data integration (Pinu et al., 2019). Specifically, Bioconductor (Gentleman et al., 2004), Galaxy (Afgan et al., 2018), GenePattern (Reich et al., 2006), Biopython (Cock et al., 2009), Pathomx (Fitzpatrick et al., 2014), SECIMTools (Kirpich et al., 2018) and more. Although multiple coding paradigms are used in bioinformatics, R and Python are essentially the lingua francas for data science analysis, where the open-source appeal and growing online community support are particularly helpful in developing a dedicated user base.

Here we introduce PyIOmica, an open source Python package, for analyzing longitudinal omics datasets, such as transcriptomics, proteomics, metabolomics etc., which includes multiple tools for processing multi-modal mapped data, characterizing time series in terms of periodograms and autocorrelations, characterizing temporal behavior, visualizing visibility graphs and testing data for gene ontology and pathway enrichment. PyIOmica includes optimized new algorithms adapted from MathIOmica (Mias et al., 2016; which runs on the proprietary Mathematica platform), now made available as Python open source code for all users, and additionally expands extensively graphical utilities for visualization of categorized temporal data, and network representation of time series. To our knowledge, there are no tools with the functionality of PyIOmica currently available in Python.

2 Materials and methods

2.1 Overview and codebase

PyIOmica provides a complete workflow for time series processing, illustrated in the Supplementary Figure S1. The modular nature of PyIOmica allows for smooth integration with any future and existing Python tools. With PyIOmica, any results can be visualized, exported and analyzed for gene enrichment by means of a user-friendly Python interface. PyIOmica’s codebase is a single Python module containing multiple groups of functions designed for annotations and enumerations, pre- and post-processing, clustering-related purposes, visualizations (heatmaps and categorization), normal and horizontal visibility graphs generation and other core and utility components. Installation is simply performed using pip install pyiomica, and package dependencies are automatically addressed directly from Python package index (PyPI). Function
PyIOmica is embedded in the module, and is easily accessible at runtime (and also at https://pyiomica.readthedocs.io). Data structures and implementation are described in Supplementary Material.

An extensive set of PyIOmica pre-processing functions enables filtering low-quality signals, tagging missing or low values, normalization, standardization, merging and comparison of the datasets. The post-processing functions, such as temporal trends categorization of power spectrum and spikes, are built on using the SciPy and scikit-learn Python toolkits. Additional functionality includes gene ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analyses for both non-temporal data, as well as for clusters identified through the automated time series categorization.

Temporal trends are automatically discovered using periodogram and autocorrelation calculations based on a Lomb-Scargle transformation algorithm (Mias et al., 2016), which properly accounts for missing points and/or unevenly sampled data. The periodogram is used to identify each time series’ underlying dominant frequencies. Autocorrelations are also used to identify how measured intensities within each time series may depend on previous measurements, by correlating a time series with delayed versions of itself. Signals showing statistically significant trends are identified for downstream analysis. Multiple omics (genes, proteins and metabolites) that show similar trends in time are identified by clustering, and can be biologically evaluated through pathway and GO analyses.

2.2 Visibility graphs and visualization

Recent work on characterizing complex events focuses on using network/graph methodology that can capture non-linear behavior (Lacasa et al., 2008). Time series are transformed into networks that conserve their topology, and allow the identification of varying temporal structures. We represent each timepoint in a series as a node. Then, for any timepoint pair with intensities \( X(t_a), X(t_b) \) at times \( t_a \) and \( t_b \), respectively, we can have an edge if for any other timepoint \( t_c \), such that \( t_a < t_c < t_b \), we have \( X(t_c) < X(t_a) + |X(t_b) - X(t_a)|/C_0 \). Representing the intensities as bars, this is equivalent to connecting the top of each bar to another top if there is a direct line-of-sight to that top. The resulting visibility graph has characteristics that reflect the equivalent time series temporal structure and can be used to identify trends. The shortest path identifies nodes (i.e. timepoints) that display high intensity, and thus dominate the global signal profile, are robust to noise, and are likely drivers of the global temporal behavior. A biological event deviating from baseline is likely to appear in one or more nodes within the shortest path.

PyIOmica uses Matplotlib plotting functions to visualize histograms, dendrograms, heatmaps and visibility graphs. Figure 1a shows example RNA-sequencing gene expression data from a 24-h time series, clustered into two groups based on autocorrelations. Subgroups were determined from the gene expression in each auto-correlation group. The data from Group 1, Subgroup 2 containing similar collective behavior over time. (a) Dendrogram with heatmap of automatically categorized longitudinal gene expression data. Autocorrelations are used to identify temporal trends in the data. Subgroups are determined based on similar collective behavior over time. (b) Visibility graph of median signal intensity from group G1S2 from (a) visualization and enrichment, and extends previous developments (Mias et al., 2016) to an open-source, community-accessible platform for data science. We anticipate future versions of PyIOmica to utilize its codebase flexibility to expand its bioinformatics tools for genomic as well as differential omics analyses, and graph construction and characterization.

Funding

This work was supported by the Translational Research Institute for Space Health through National Aeronautics and Space Administration (NASA) Cooperative Agreement NNX16AO69A.

Conflict of Interest: G.M. has consulted for Colgate-Palmolive North America. C.P. owns equity in Salgomed, Inc. S.D. reports no potential conflict of interest.

References

Afgan,E. et al. (2018) The Galaxy platform for accessible, reproducible and collaborative biomedical analyses: 2018 update. Nucleic Acids Res., 44, W537–W544.

Chen,R. et al. (2012) Personal omics profiling reveals dynamic molecular and medical phenotypes. Cell, 148, 1293–1307.

Cock,P.J.A. et al. (2009) Biopython: freely available Python tools for computational molecular biology and bioinformatics. Bioinformatics, 25, 1422–1423.

Fitzpatrick,M.A. et al. (2014) Pathomx: an interactive workflow-based tool for the analysis of metabolomic data. BMC Bioinformatics, 15, 396.

Garrett-Bakelman,F.E. et al. (2019) The NASA Twins Study: a multidimensional analysis of a year-long human spaceflight. Science, 364, 6436.

Gentleman,R.C. et al. (2004) Bioconductor: open software development for computational biology and bioinformatics. Genome Biol., 5, R80.

Kirpich,A.S. et al. (2018) SECIMTools: a suite of metabolomics data analysis tools. BMC Bioinformatics, 19, 151.

Lacasa,L. et al. (2008) From time series to complex networks: the visibility graph. Proc. Natl. Acad. Sci. USA, 105, 4972–4975.

Mias,G.I. et al. (2016) Mathionica: an integrative platform for dynamic omics. Sci. Rep., 6, 37237.

Pinu,F.R. et al. (2019) Systems biology and multi-omics integration: viewpoints from the metabolomics research community. Metabolites, 9, 76.

Price,N.D. et al. (2017) A wellness study of 108 individuals using personal, dense, dynamic data clouds. Nat. Biotechnol., 35, 747.

Reich,M. et al. (2006) GenePattern 2.0. Nat. Genet., 38, 500–501.