Analysis of genetic variation and potential applications in genome-scale metabolic modeling

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Genetic variation is the motor of evolution and allows organisms to overcome the environmental challenges they encounter. It can be both beneficial and harmful in the process of engineering cell factories for the production of proteins and chemicals. Throughout the history of biotechnology, there have been efforts to exploit genetic variation in our favor to create strains with favorable phenotypes. Genetic variation can either be present in natural populations or it can be artificially created by mutagenesis and selection or adaptive laboratory evolution. On the other hand, unintended genetic variation during a long term production process may lead to significant economic losses and it is important to understand how to control this type of variation. With the emergence of next-generation sequencing technologies, genetic variation in microbial strains can now be determined on an unprecedented scale and resolution by re-sequencing thousands of strains systematically. In this article, we review challenges in the integration and analysis of large-scale re-sequencing data, present an extensive overview of bioinformatics methods for predicting the effects of genetic variants on protein function, and discuss approaches for interfacing existing bioinformatics approaches with genome-scale models of cellular processes in order to predict effects of sequence variation on cellular phenotypes.

General information
State: Published
Organisations: Novo Nordisk Foundation Center for Biosustainability, iLoop, Department of Systems Biology, Network Engineering of Eukaryotic Cell Factories, Research Groups
Contributors: Cardoso, J., Andersen, M. R., Herrgard, M., Sonnenschein, N.
Number of pages: 12
Publication date: 2015
Peer-reviewed: Yes

Publication information
Journal: Frontiers in Bioengineering and Biotechnology
Volume: 3
Issue number: 13
Ratings:
Web of Science (2019): Indexed yes
Web of Science (2018): Indexed yes
Scopus rating (2017): CiteScore 4.36 SJR 1.565 SNIP 1.175
Web of Science (2017): Indexed yes
Scopus rating (2016): CiteScore 1 SJR 1.347 SNIP 0.794
Scopus rating (2015): SJR 1.16 SNIP 0.767
Scopus rating (2014): SJR 0.415 SNIP 2.4
Original language: English
Keywords: Genetic variation, SNP, Next-generation sequencing, Constraint-based modeling, Metabolic engineering, Adaptive laboratory evolution, Metabolism, High-throughput analysis
Electronic versions:
Analysis_of_genetic_variation_and_potential_applications.pdf
DOIs:
10.3389/fbioe.2015.00013

Bibliographical note
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Source: PublicationPreSubmission
Source-ID: 110377311
Research output: Research - peer-review › Journal article – Annual report year: 2015