Blue light phototherapy for Psoriasis from a systems biology perspective

One approach to lessen both these problems is to analyse such large datasets in the context of what we already know. Biologists often use pathways to explain and visualize what is known about biological processes. Pathways are used for instance in papers, presentations, and textbooks. Some well-known web resources for computer readable versions of biological pathways are KEGG, Reactome, and our own WikiPathways. These pathways are biological data models but connection of experimental data to such pathway models needs mapping. Typically both the entities in experimental data that we want to analyse and the "same" entities in pathways have some kind of associated database identifiers. But these identifiers are often from different databases and sometimes not even describing the exact same entity. The use of a microarray probe set identifier reporting for mRNA expression while the pathway contains protein identifiers is a typical example. Such mappings are in fact needed for almost every data integration step. BridgeDb is used for identifier mapping in our pathway tool PathVisio and in WikiPathways. It can also be used in tools like Cytoscape, Bioconductor/R, Open PHACTS or as a web service. Using this we can perform pathway enrichment statistics and pathway data visualization for any kind of gene product or for metabolomics data.
Two new developments allow us to combine these pathway approaches with mathematical modelling. With the SBML converter mathematical models can be converted into WikiPathways pathway format. With a flux/interaction visualization plugin for PathVisio, modelling results can be visualized on these pathways. This, of course, also needed new identifier mapping databases for biological reactions. One big advantage is that visual representations of models can now be updated automatically with the model itself, which makes a critical evaluation of the models much easier. The other advantage is of course that experimental data can be combined with modelling results and visualized on the same pathway model representation. Modelling of effects of measured transcriptomics changes on predicted enzyme kinetics could thus for instance be combined with actual and predicted metabolite concentrations all in one pathway.
Still, neither pathway nor simulation models can contain all the known regulatory interactions for the processes they describe. That is why we will often want to use network biology approaches to extend pathways dynamically with things like directly interacting proteins, transcription factors, regulatory RNAs, or drugs. With the WikiPathways plugin for Cytoscape we can analyse pathways, including the SBML converted models, as networks and thus use network approaches to evaluate which regulatory processes might affect the models studied. Effectively this connects another big data world to data modelling and simulations.
All these approaches will become even more powerful if we learn to integrate data about genetic variations better. Once we learn to map genetic changes to the specific interactions that they affect in a biological network we learn to understand how different variations affecting the same process can lead to epistatic interactions or how specific variations in the same gene can lead to "edgetics" because they affect different edges in the network underlying the pathway. To do this we have to integrate tools that predict effects of genetic variations on specific interactions to "move" these gene related variations to the edges that they affect. Combining all the aspects described above we could also model the effects of such changes in interactions caused by genetic variations and use that for predictions.
Of course the things described in the last paragraphs are still futuristic in part. But many of the needed steps can already be made. As usual the path is easier to find if you walk it backwards. Converting a mathematical model to a pathway allows evaluation of different types of experimental data and modelling results in the same context. The maze is completed by adding regulatory information and genetic data affecting interactions. Both these types of added information can then be evaluated through changes made in the mathematical model or its parameters. We need to learn to walk all the steps that form this path, instead of focussing on single steps. In this way biologists may still learn how to fix a radio.

Félix Garza, Zandra C.

Blue light phototherapy for Psoriasis from a systems biology perspective

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This work analyses the effect of UV-free blue light (BL) irradiation of the skin using mathematical modelling. Prior research has shown that blue light reduces the proliferation of keratinocytes by inducing their differentiation, and causes apoptosis of lymphocytes. The effects of blue light on these cells make it an attractive phototherapy alternative for inflammatory skin conditions, such as psoriasis. Nevertheless, the exact process by which BL affects these cells is not fully understood. A modelling approach may give further insight to understanding how BL irradiation of psoriatic skin leads to the control of the disease. However, no mathematical model is available describing this phenomenon. Two deterministic models were therefore made to describe the epidermal kinetics and interaction between keratinocytes and lymphocytes under the effect of BL irradiation; focusing mainly on the case of psoriasis. We employed a systems biology approach to characterize the effect of BL irradiation of the skin. Since in phototherapy parameters such as fluence and power have a strong impact on the outcome, a parameter sensitivity analysis (PSA) was performed to estimate a range of fluence and power at which BL phototherapy could be successful. The models results suggest that the management of psoriasis is achieved by inducing symmetric differentiation of the keratinocytes in the epidermal proliferative compartment. It is observed that BL irradiation of psoriatic skin decreases the density of keratinocytes and transiently increases the density of lymphocytes, leading to the regulation of the interaction between these two cell types. The PSA of the models predicts that the higher the peak power the better the outcome of the BL phototherapy with a dose of 90J/cm2 per day. This systems biology approach provides additional insight into the use of BL phototherapy for inflammatory skin disorders.

Franke, Lude — Invited Speaker

Identification of downstream effects for many genetic risk factors by reanalysing gene expression data

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Text TBA

Greef, Jan van der — Invited Speaker

East is East and West is West: and never the twain shall meet?

Jan van der Greef

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The shift from a reductionistic towards a systems view is globally a key topic in Life Sciences. System-based approaches need the understanding of the interconnectivity of systems and the organizing principles.