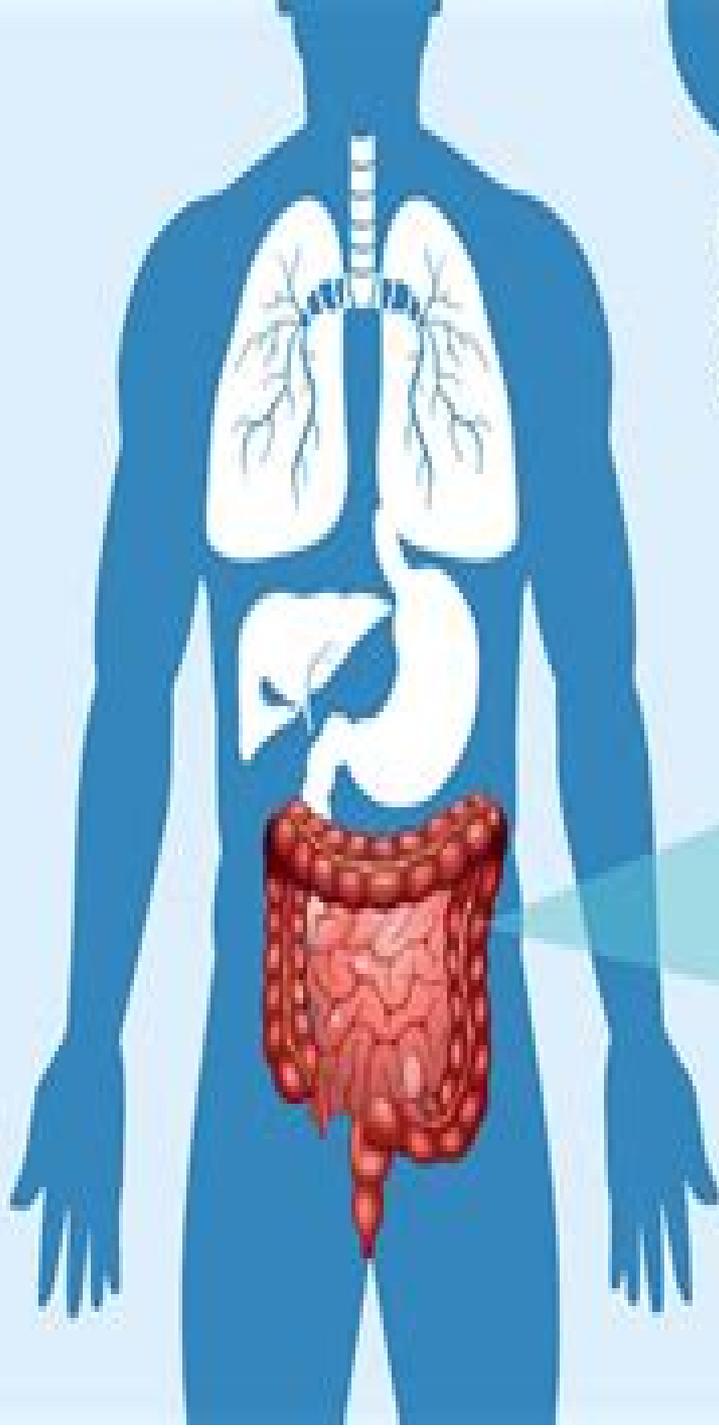


# Inflammatory Bowel Disease (IBD)

Inflammatory Bowel Disease (IBD) is a group of chronic inflammatory conditions that affect the digestive tract, including Crohn's disease and ulcerative colitis.



Normal colon



Ulcerative colitis



Crohn's disease

# Software Costing Ibd 1 E

**Guillaume Favre**



## Software Costing Ibd 1 E:

*The Software Encyclopedia 2001*, 2001 *Adweek*, 1999 *Drug Intelligence & Clinical Pharmacy*, 1987 National Library of Medicine Audiovisuals Catalog National Library of Medicine (U.S.), 1992 **Logical Modeling of Cellular**

**Processes: From Software Development to Network Dynamics** Matteo Barberis, Tomáš Helikar, 2019-08-16

Mathematical models have become invaluable tools for understanding the intricate dynamic behavior of complex biochemical and biological systems. Among computational strategies, logical modeling has been recently gaining interest as an alternative approach to address network dynamics. Due to its advantages including scalability and independence of kinetic parameters, the logical modeling framework is becoming increasingly popular to study the dynamics of highly interconnected systems such as cell cycle progression, T cell differentiation, and gene regulation. Novel tools and standards have been developed to increase the interoperability of logical models which can now be employed to respond to a variety of biological questions. This Research Topic brings together the most recent and cutting edge approaches in the area of logical modeling including, among others, novel biological applications, software development, and model analysis techniques. *Construction and utilization of digital twins for personalized therapeutic predictions* Samuel Schäfer, 2024-10-18. Modern healthcare faces a significant challenge, namely that 25-70% of patients with common diseases do not benefit from standard treatments despite the availability of over 13,000 drugs registered in DrugBank. This discrepancy is likely due to these diseases' complex and heterogeneous molecular nature rather than a lack of therapeutic options. Emerging technologies have revealed the immense molecular complexity underlying common diseases. For instance, single-cell RNA sequencing (scRNA-seq) has demonstrated altered gene interactions in and across multiple cell types in numerous tissues. Furthermore, these technologies have revealed vast molecular differences between patients with the same diagnosis. There is a wide gap between this complexity and the current diagnostic and therapeutic approaches. Aim: To bring personalized medicine one step closer to the clinic, this thesis focuses on developing digital disease models that can capture the molecular biological complexity of disease in individual patients. We aim to harness these disease models to identify optimal treatments for each individual patient. Paper I: We started by exploring the usefulness of OMIC-based approaches for diagnostic and therapeutic predictions. Utilizing a single-cell RNA sequenced mouse model of antigen-induced arthritis, we aimed to prioritize cell types and therapeutic targets. Initial pathway enrichment analyses did not yield relevant prioritization, prompting an investigation into network-based approaches. Multi-cellular disease models (MCDMs) for AIA and human rheumatoid arthritis were constructed, incorporating predicted cell type interactions. Centrality analysis indicated that these interactions could quantify a cell type's relative importance in disease pathogenesis. We hypothesized that transcriptomic alterations in central cell types might reflect the MCDM serving as potential diagnostic markers. An analysis of CD4 T cells from patients with 13 different inflammatory diseases and healthy controls demonstrated that these profiles could discriminate between healthy and diseased states and among diseases.

Furthermore a network based approach identified drugs targeting disease associated changes common to multiple inflammatory diseases Notably one of these drugs bezafibrate successfully dampened inflammation in the AIA mouse model Paper II Building on the insights from Paper I we investigated multicellular network models MNMs with time as an additional dimension Using seasonal allergic rhinitis SAR as a disease model we analyzed time series scRNAseq data to construct MNMs of inflammatory diseases We identified thousands of disease associated expression changes across multiple cell types varying at different disease stages Notably upstream regulators URs of these changes were also stage dependent and multidirectional To prioritize URs for drug discovery we focused on those causing significant expression changes in multiple cell types across all time points This strategy was validated through similar analyses of atopic dermatitis ulcerative colitis and Crohn s disease confirming that ranked URs aligned with the efficacy of existing drugs targeting the URs in the respective diseases Furthermore experimental validation included targeting the top ranked regulatory gene in SAR which was more effective than previously discovered IL4 inhibition Paper III While Paper I established the use of transcriptomic data for therapeutic predictions it focused on overlapping disease related changes across multiple inflammatory diseases and considered transcriptomic changes in only one cell type Paper II indicated a potential benefit in UR prioritization in numerous cell types However it yielded heterogeneous results and was limited by the fact that few drugs directly target URs Neither of these approaches was feasible for individualized drug predictions Drawing on previous insights by us and others we next aimed to develop digital disease models for individual patients termed digital twins with the capability for drug efficacy screening We proposed scDrugPrio a strategy utilizing single cell scRNA sequencing based multicellular disease models incorporating key biological and pharmacological properties such as varying gene expression levels varying gene interactions within and between cell types and drug effect scDrugPrio was constructed based on a mouse model of arthritis and validated by improved precision recall for known drugs and in vitro studies of predicted drugs that were FDA approved for other diseases and had not yet been tried in rheumatoid arthritis or mouse arthritis For validation scDrugPrio was applied to human multiple sclerosis as well as Crohn s disease data that included tissue samples from healthy and sick tissue of all patients scDrugPrio was able to identify relevant treatments for individual patients and could distinguish anti TNF responders from non responders Conclusion This thesis demonstrates a framework for constructing digital disease models for personalized therapeutic predictions that might hold potential for better clinical treatment decisions By leveraging advanced genome wide analyses and network based approaches we may enhance the precision and efficacy of treatments for immune mediated inflammatory diseases bringing personalized medicine closer to clinical reality

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