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Artificial neural network algorithms for biomarker discovery, pathway modelling and drug target identification

Cancer is a complex disease with a myriad of forms and prognoses occurring within each type. For example, in breast cancer using genomic profiling in excess of 80 sub types have been identified. The ability to characterize the disease for each patient may offer the potential to assess the molecular sub-type of the disease and thus accurately determine the patients' prognostic outcome. Methodologies such as mass spectrometry-based proteomics, RNA-Seq and gene expression arrays offer the potential for characterization of disease derived samples using a huge number of proteins or genes. This depth of information while providing a comprehensive overview of a disease state also proves problematic in its complexity. One has to search through potentially hundreds of thousands of pieces of information for consistent features that address a clinical question in the population. The human mind is very good at finding patterns in a system but is not able to conduct the task repetitively for large numbers of parameters. Conversely computers are very good at searching for features in such a data space, but previously defined statistical methods are not able to cope with the high complexity. Here we present the application of artificial neural networks (ANNs, a form of artificial intelligence having the characteristics of both human pattern recognition and computer automated searching) to finding genomic solutions to questions in cancer. We also present the use of a range of statistical and artificial intelligence-based machine learning techniques to develop prognostic models for breast cancer. Results of use of ANN algorithms for biomarker discovery, pathway modelling and molecular driver (putative drug target) identification; a parallel analysis of multiple molecular databases for breast cancer identification of markers that drive proliferation and thus predict response to anthracycline through network inference techniques will be presented.

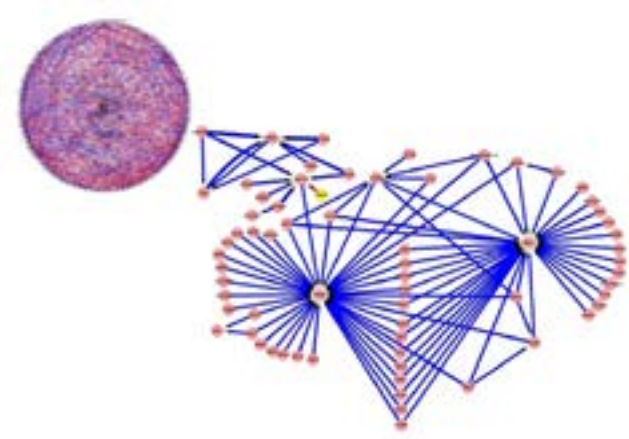

Figure 1: Network inference identifies key drivers of proliferation in breast cancer

Recent Publications:

1. Tarek M A Abdel Fatah et al. (2016) SPAG5 as a prognostic biomarker and chemotherapy sensitivity predictor in breast cancer: a retrospective, integrated genomic, transcriptomic and protein analysis. The Lancet Oncology. 17(7):1004-1018. Doi:10.1016/S1470-2045(16)00174-1.
2. Tarek M A Abdel Fatah et al. Nottingham clinico-pathological response index (NPRI) after neoadjuvant chemotherapy (Neo-ACT) accurately predicts clinical outcome in locally advanced breast cancer. Clinical Cancer Research. 21(5):1052-1062. Doi:10.1158/1078-0432.CCR-14-0685.
3. T M A Abdel Fatah et al. (2013) Bcl2 is an independent prognostic marker of triple negative breast cancer (TNBC) and predicts response to anthracycline combination (ATC) chemotherapy (CT) in adjuvant and neoadjuvant settings. Annals of Oncology. 24(11):2801-2807. Doi:10.1093/annonc/mdt277.
4. Roger W McGilvray et el. (2009) NKG2D ligand expression in human colorectal cancer reveals associations with prognosis and evidence for immunoediting. Clinical Cancer Research. 10/2009; 15(22):6993-7002. Doi:10.1158/1078-0432.CCR-09-0991.
5. L J Lancashire et al. (2009) A validated gene expression profile for detecting clinical outcome in breast cancer using artificial neural networks. Breast Cancer Research and Treatment. 120(1):83-93. Doi:10.1007/s10549-009-0378-1.

Biography

Graham Ball pursued his PhD in Informatics (UN funded) and a Postdoc in modelling environmental interactions with ANNs at Nottingham Trent University (NTU) UK in 2000. His work focuses on analysis of proteomic and transcriptomic data; searching for proteins and genes associated with cancer. He is currently a Professor of Bioinformatics at Nottingham Trent University and CSO of CompanDX UK Ltd, UK respectively. He is also an Associate Director at the John Van Geest Cancer Research Centre (UK) and biostatistics lead on three clinical projects. He has been involved in the development and validation of machine learning algorithms based on artificial neural networks (ANNs) for the past 18 years. He has 145 journal papers and 5 patents in this area. His current research interests are directed at the use of machine learning techniques for the identification of biomarker panels, pathway motifs and molecular drivers characterizing biological systems. These include areas such as microbial pathogen host response, drivers and characteristics of hallmarks of cancer, drivers of Alzheimer's disease and diagnostics of latent tuberculosis.

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