Comparative Cancer Genomics via Multiresolution Network Models

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Abstract

Genome-wide network models of multi 'omics cancer data are popular tools for studying and revealing both unique and shared mechanisms across malignancies. We have previously studied such "pan-can" (multi-cancer) models using sparse inverse covariance selection (SICS) (Kling et al, 2015). While our SICS model is a highly useful tool for data integration, there are important questions that warrant further study. First, the large number of co-linear variables creates instability of network estimation. When no clear "winning" model comes out of estimation, these large networks are difficult to interpret or, worse still, simply speculative. Secondly, while model estimation is based on highly optimized solvers, improvements of scalability are needed to handle future data sets. We therefore propose multi-resolution SICS (MR-SICS), designed to adaptively aggregate the data into interpretable components, as part of the network construction. MR-SICS builds on a nested latent model formulation of network components. At each level of resolution of the model, the parameters for comparative inference are relatively small, substantially improving estimation stability and interpretability. In addition, the multiresolution representation simplifies interactive viewing and analysis of the models. We demonstrate MR-SICS on simulated data as well as cancer 'omics data.

References

1. T. Kling and P. Johansson and J. Sanchez and V.M. Marinescu and R. Jörnsten and S. Nelander . Efficient exploration of pan-cancer networks by generalized covariance selection and interactive web content . Nuclear Acids Research 43(15), e98, 2015 gkv413.