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Omic fold changes clustering with alignment and network inference: an application to study the radiation response of endothelial cells

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Radiotherapy is a type of cancer treatment that may induce adverse effects for healthy tissues situated close to the irradiated tumor. It is important to study and compare different modes of radiotherapy in order to select those minimizing the potential undesirable consequences. This work focuses on the response of endothelial cells, key actors in the appearance of radiation adverse effects. We study the expression of genes originating from transcriptomic in-vitro datasets that were collected for several time points under irradiated and non-irradiated conditions. The goal is to determine a small number of the most representative behavior types among all considered genes, and to identify potential biological pathways linked to the response to radiotherapy. The quantity of interest is radio-induced fold change: a measure of irradiation effect represented by the difference between the two experimental conditions over time. We propose a new approach based on modeling fold changes as random variables, and a new distance that allows to account for uncertainties and correlations between variables. We designed a computationally efficient procedure performing simultaneous clustering and alignment of fold changes' random estimators. Based on the obtained information, a gene network is inferred allowing to draw a comparison between different modes of radiotherapy.

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