i-Cellulo: a SaaS platform for the automatic statistical analysis of cell impedance signals
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Objectives. Label-free methods such as cell impedance assays are in vitro tests increasingly used in drug development. An indirect difficulty with those technologies is the large amount of kinetic responses to be processed. Our objective is to automate the processing and analysis of those data with a web computational server available to all biologists and able to perform multivariate tests, response profile clustering and dynamic AC50 estimation.

Methods

The proposed solution relies on a SaaS platform in which R-language algorithms have been implemented for the on-line processing of cell impedance signals. Three generic statistical problems are addressed: clustering of response profiles to screen compounds, multivariate testing to compare their activity and AC50 estimation to determine their concentration effects. ANOVA, Kruskall-Wallis and Tuckey’s range tests have been implemented for the multivariate testing. Hierarchical clustering based on Singular Spectrum Analysis were used for the non-supervised response profile classification. A Hill’s model structure and a maximum likelihood estimator were adopted for the AC50 calculation.

Results

Hundreds of tests were carried out on real in vitro signals to assess the practical relevance of i-Cellulo for the fast analysis and characterization of anti-cancer activities in early steps of drug development. Results clearly show the ability of this web-based solution to correctly discriminate, classify, compare and rank the anti-cancer responses of tested compounds compared to gold standards.

Conclusion

With the advent of real-time cell measurement technologies in preclinical tests, new services for the analysis of high-content data are needed. i-Cellulo is a solution to that challenge and allows biologists to speed up their data analysis and facilitate interpretation of their results.

Fig.1: Comparing 2 groups of cell impedance profiles. Left: original CI responses to be compared. Right: t-Test results.

Fig.2: Multiple test of CI responses. Left: groups of CI responses to be compared. Right: ANOVA results.

Fig.3: Clustering Cell Index Profiles for Screening Applications. Left: dendrogram of culture wells. Right: 3 clusters of response.

Fig.4: Estimation of the AC50 profiles. Left: AC50 values estimation based on the Hill’s model. Right: time profile of the AC50 estimates.