# Deconvolution of drug-response heterogeneity in cancer cell populations

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Ex vivo drug-sensitivity assays are a basic component of biomedical research. Typically, cells are treated with varying drug concentrations and viable cells are measured at one or more time points. Viability curves, and their characteristics (e.g. IC50), allow to compare drug sensitivity across multiple drugs and cell samples. However, the interpretation of those curves is confounded by the presence of cellular heterogeneity in each sample. The presence of several subclones with different drug sensitivities results in an aggregated drug sensitivity profile that does not represent the cell population complexity, and thus hinders the design of precise treatment strategies.

In this talk I will show how to infer on the presence of cellular subclones with differential drug response, using standard cell viability data at the total population level. We build cell population dynamic models of the evolution of individual subclones over time and dose. We estimate the number of subclones, their proportion and drug-response profiles. We validate the methodology on viability data from admixtures of synthetic and actual cancer cell lines at various known frequencies. Finally, we explore the clinical usefulness of the method by deconvolving drug-response heterogeneity in multiple myeloma patient samples.

This is joint, ongoing work with Jasmine Foo, Kevin Leder and Jasmine Noory (University of Minnesota); Arnoldo Frigessi and Even M. Myklebust (University of Oslo); Shannon M. Mumenthaler (University of Southern California); Dagim. S. Tadele (Cleveland Clinic and Oslo University Hospital), Mariaserena Giliberto, Fredrik Schjesvold, Jorrit Enserink and Kjetil Tasken (Oslo University Hospital).