

"Borrowing Strength with Non-Exchangeable Priors over Subpopulations"

We introduce a non-parametric Bayesian model for phase II clinical trial with patients presenting different subtypes of the disease under study. The subtypes are not a priori exchangeable. The lack of a priori exchangeability hinders the straightforward use of traditional hierarchical models to implement borrowing of strength across disease subtypes. We introduce instead a random partition model for the set of disease subtypes. All subtypes within the same cluster share a common success probability. The random partition model is a variation of the product partition model that allows us to model a non-exchangeable prior structure.

In particular the data arises from a phase II clinical trial of patients with sarcoma, a rare type of cancer affecting connective or supportive tissues and soft tissue (e.g., cartilage and fat). Each patient presents one subtype of the disease and subtypes are grouped by good, intermediate and poor prognosis. The prior model should respect the varying prognosis across disease subtypes. Two subtypes with equal prognosis should be more likely a priori to co-cluster than any two subtypes with different prognosis. The practical motivation for the proposed approach is that the number of accrued patients within each disease subtype is too small to assess the success rates with the desired precision if we were to analyze the data for each subtype separately. It would be practically impossible to carry out a clinical study of possible new therapies.

Like a hierarchical model, the proposed clustering approach considers all observations, across all disease subtypes, to estimate individual success rates. But in contrast with the standard hierarchical models, the model considers disease subtypes a priori non-exchangeable. This implies that when assessing the success rate for a particular type our model borrows more information from the outcome of the patients sharing same prognosis than from the others.