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Inferring clonal mutations from a spatial computational model of intratumour heterogeneity

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The discovery of cancer heterogeneity and clonal evolution added a further layer of complexity upon biology of cancer and its treatment. Thus, ability to correctly distinct clonal from subclonal mutations became important for making the right therapeutic choice. Here, we investigate underlying causes of sampling bias and the effects spatial distribution and size of samples have on the ability to identify truly clonal alteration from multi-region profiling of tumours. To test that, we simulated neoplastic growth together with spatial tumour heterogeneity and subjected it to different sampling strategies. Using that approach we found that the frequency of first subclonal mutation is the main factor which determines the accuracy of truncal mutation estimation in structured tumour. We also found that higher spatial dispersion of the biopsies and their smaller sizes increase the accuracy of the estimations. Thus we propose to take those features into consideration during sampling process.