Universität Regensburg

FAKULTÄT
MEDIZIN
Institut für Funktionelle Genomik
Lehrstuhl für Statistische Bioinformatik

Regensburg Lectures in Medical Bioinformatics

"Computational methods for the analysis of intra-tumour heterogeneity in single-cell dnaSeq data"

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Introduction

The mutational heterogeneity observed within tumours is a key obstacle to the development of effective cancer therapies. A thorough understanding of subclonal tumour composition and the underlying mutational history is essential to the design of treatments tailored to individual patients. Present studies on tumour evolution are primarily based on sequencing data obtained from bulk tumour tissue that is comprised of hundred thousands or millions of cells. The admixed mutation profiles obtained in such studies often underestimate the mutational heterogeneity of a tumour.

Through recent technological advances it is now possible to sequence the DNA of individual cells. This opens up not only the possibility to analyse the evolutionary history of tumours at an unprecedented resolution but also to leverage the potential of circulating tumour cells whose mutational profiles are of particular interest to the analysis of metastatic seeding patterns. The transition from bulk to single-cell sequencing data poses a number of statistical challenges such as elevated noise rates due to allelic drop out, missing data and contamination with doublet samples.

We developed a Bayesian inference scheme for tumour mutation histories based on single-cell sequencing data [Jahn et al., 2016]. In this talk I will focus on two recent extensions of this work, a novel single-cell mutation caller that takes the underlying cell phylogeny into account [Singer et al., 2018] and a statistical test to identify parallel mutations and mutation loss [Kuipers et al., 2017]. Our results on simulated and real tumour data show that a thorough modelling of the noise inherent to single-cell data allows for an accurate reconstruction of tumour mutation histories.

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