

Using Computational Algebraic Topology to Characterize Chromosomal Instability in Cancer

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Abstract: DNA copy number aberrations (CNAs) are often associated with cancer initiation and progression and can be detected using microarray technologies. We propose a method Multidimensional Analysis of CGH (MDACGH), which draws from the theory of computational algebraic homology to find recurrent CNAs. Applying this method, we show that MDACGH analysis of 147 primary glioblastoma tumor samples published by the TCGA network detects all reported deletions and 60% of the amplifications while using a subset of the samples. It also finds two new regions of CNAs on arms 5q and 18p not previously reported by TCGA. We also applied MDACGH to the Climent et al. breast cancer dataset, with the goal of finding CNAs associated with disease recurrence. MDACGH finds two novel regions of CNAs (1q and 6q) that were not found by the original study. The current implementation of MDACGH combines the results for all dimensions into a single p-value. We hypothesize that there is a relationship between the size of the aberration and the dimension at which the difference between 0 curves are significant. We performed simulations and tested different combinations of amplifications from dimension 2 to 10 and found that dimensions smaller than the size of the aberration had significant p-values while larger ones lost significance. Some CNAs may occur in combination rather than independently. Higher order homology, such as the first homology group that computes two-dimensional holes in the cloud of points, has the potential to detect more complex interactions, including these combinations.

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