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Sparse Modelling of Cancer Patients' Survival Based on Genomic Copy Number Alterations

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Abstract : Copy number alterations (CNA) are variations in the structure of the genome, where certain regions deviate from the typical two chromosomal copies. These alterations are pivotal in understanding tumor progression and are indicative of patients' survival outcomes. However, effectively modeling patients' survival based on their genomic CNA profiles while identifying relevant genomic regions remains a statistical challenge. Various methods, such as the Cox proportional hazard (PH) model with ridge, lasso, or elastic net penalties, have been proposed but often overlook the inherent dependencies between genomic regions, leading to results that are hard to interpret. In this study, we enhance the elastic net penalty by incorporating an additional penalty that accounts for these dependencies. This approach yields smooth parameter estimates and facilitates variable selection, resulting in a sparse solution. Our findings demonstrate that this method outperforms other models in predicting survival outcomes, as evidenced by our simulation study. Moreover, it allows for a more meaningful interpretation of genomic regions associated with patients' survival. We demonstrate the efficacy of our approach using both real data from a lung cancer cohort and simulated datasets.

Keywords : copy number alterations, cox proportional hazard, lung cancer, regression, sparse solution
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