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AI and Quantum Research Center (AIQRC), Asia University, Taiwan

Activities

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INTERNATIONAL SYMPOSIUM ON HUMANOID ROBOTICS AND SOVEREIGN AI FOR FUTURE LIVING, Asia University

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INTERNATIONAL SYMPOSIUM ON HUMANOID ROBOTICS AND SOVEREIGN AI FOR FUTURE LIVING

From Single Cells to Populations: A QUBO/Quantum Annealing Blueprint for Translational Biomarker Discovery

Tumors are mosaics of malignant, immune, and stromal cells. Bulk RNA-seq, while central to many clinical studies, averages signals across these compartments and obscures mechanism. Single-cell RNA sequencing (scRNA-seq) restores cellular resolution but suffers from modest sample sizes and substantial technical noise. The clinically credible path is integration: learn high-fidelity, cell-type–specific features from single cells, then stress-test them across population-scale bulk cohorts.

Stage 1 — Cell-type–resolved discovery (single-cell stage).

Within annotated cell populations, candidate biomarkers are selected with a mutual-information–based, redundancy-aware objective. The objective is cast as a Quadratic Unconstrained Binary Optimization (QUBO) and solved via hybrid quantum annealing, favoring compact gene sets that are simultaneously informative and non-redundant—essential for generalization. Compared with LASSO or black-box ensembles, QUBO selection can uncover nonlinear gene–phenotype relationships and "master regulators" that might otherwise be underweighted.

Stage 2 — Cohort-scale validation (bulk stage).

Single-cell signatures are projected into bulk cohorts using deconvolution-aware scoring, then tested for association with outcomes (e.g., response, time-to-event) under proper covariate adjustment. This step quantifies clinical relevance, transportability across platforms and centers, and effect robustness at population scale.

QUBO algorithm

The algorithm embraces two hard constraints of biomedicine—high dimensionality and interacting signals—by balancing feature–target importance (mutual information) against feature–feature redundancy within a single energy landscape. The annealer explores many combinatorial subsets efficiently and converges on stable, sparse panels. Empirically, QUBO recovers nonlinear

ground-truth features in simulations; identifies differentiation and drug-resistance genes missed by conventional methods; and exhibits strong cross-validated stability—properties that translate into more reliable transfer of single-cell signatures into bulk cohorts.

Biomedical, clinical, and computational payoffs.

Single-cell discovery isolates cell-intrinsic programs while filtering microenvironmental confounders; QUBO attenuates co-regulated redundancies. Bulk-cohort validation scales signals to thousands of patients, yielding hazard-ratio and response-rate evidence rather than effect sizes from small single-cell sets. Hybrid quantum/classical solvers navigate rugged feature landscapes without the exhaustive cost of greedy wrappers and outperform purely linear sparsifiers when relationships are nonlinear.

Case insight.

QUBO-selected panels captured endothelial differentiation programs (e.g., Wnt/VEGF axis members) and time-dependent drug-tolerance trajectories in lung cancer, including resistance-linked regulators overlooked by standard pipelines—demonstrating mechanistic specificity and discovery breadth. By pairing single-cell precision with bulk-cohort power—and replacing ad-hoc curation with a principled QUBO/quantum annealing optimizer—this framework yields biomarker panels that are compact, mechanistically grounded, and clinically testable, reducing noise, increasing robustness, and accelerating translation from granular biology to population-level impact.

Click here to read more.

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