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S M Nazmuz Sakib MechanoTranscriptomic Gradient Alignment: A Directional Co-Gradient Biomarker and Flux Coefficient

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Background: We introduce the S M Nazmuz Sakib MechanoTranscriptomic Gradient Alignment (MTGA) framework for solid tumors, formalizing a directional coupling between tissue stiffness gradients and malignant cell-state gradients.

Methods: The core statistic, the Sakib Alignment Index κS, averages the local cosine of the angle between ∇E stiffness) and ∇S (cell-state score) with scale-aware weighting; the companion Sakib Flux Coefficient µS estimates a signed mechanosensitivity slope relating ∇S to ∇E. We describe multi-scale estimation, spatially autocorrelated nulls, registration/stability diagnostics, and edge-versus-core enrichment.

Results: Using synthetic data and analysis-ready plotting primitives, we provide ten ready-to-compile illustrations.

Conclusion: Contextualized against durotaxis and spatial transcriptomics, and recent mechanotranscriptomic analytics, the framework appears conceptually novel: prior work studied stiffness heterogeneity and gene-expression gradients, but not a single directional alignment index nor a signed flux fit across tumor sections. We outline how to apply MTGA on AFM/MRE/SHG or force-inference layers co-registered to Visium-like grids, with spatially-constrained nulls via Moran spectral randomization.

Introduction

Tumors exhibit spatial heterogeneity in extracellular matrix (ECM) stiffness that affects invasion, EMT, and therapy response [1-4, 5-9]. Durotaxis migration along stiffness gradients has been demonstrated at cell and tissue scales. In parallel, spatial transcriptomics (ST) routinely reveals core-to-edge gene-expression architectures predictive of outcomes. While computational alignment of ST datasets is advancing, and mechanotranscriptomic integration at single-cell resolution is emerging, a directional co-gradient scalar summarizing alignment between ∇E (stiffness) and ∇S (cell state) across a tumor section has not been formalized [1-4].

The S M Nazmuz Sakib MTGA Framework

Definition 1 (Sakib Alignment Index κS). On a tissue domain Ω with stiffness map $E(x)$ and cell-state score with $\kappa S \in [-1,1]$; +1 indicates perfect co-alignment and -1 anti-alignment. Here $w(x)$ weights (e.g., tumor mask × spot density), and $(\alpha, \beta) \geq 0$ emphasize informative gradients.

x μ x x Definition 2 (Sakib Flux Coefficient μS (Directed Mechano-Transcriptomic Flux)). Estimate the signed gain linking ∇S to ∇E by the least-squares fit $\mu S = \arg\min \sum w(x) \|\nabla S(x) - \mu \nabla E(x)\|2 = (\sum w(x) \nabla E \cdot \nabla S) / (\sum w(x) \|\nabla E\|2)$. μS has units of S per stiffness and complements κS (direction vs. gain). Report with R^2 and a spatially-aware p-value.

S M Nazmuz Sakib Principle 1 (Multi-scale MTGA). Compute $\kappa\_S(\sigma)$ after smoothing (E,S) with scale σ; summarize via the scale-integrated index $siMTGA = 1/|\Sigma|$

$\sum(\sigma \in \Sigma) \kappa S(\sigma)$ (log-spaced Σ), revealing whether coupling is fine-grained (edge) or coarse (tissue-level).

S M Nazmuz Sakib Hypothesis 1 (Edge Enrichment). κS is elevated within a finite band of the invasive edge relative to the tumor core in cancers with durotaxis- consistent programs.

Data Layers and Registration

Mechanics layer $E(x)$. Direct stiffness maps can be obtained by AFM on sections or via ex vivo SIM-AFM co-registered to fluorescence. When unavailable, stiffness proxies from SHG/collagen organization or force-inference tensors can be used [4, 10 ,11].

Omics layer $S(x)$. Choose a scalar cell-state (EMT, stemness, hypoxia, pseudotime, therapy-response metagene). ST registration. Align mechanical and ST grids with diffeomorphic tools (e.g., STalign) [12, 13].

Estimation, Inference, and Stability

Compute ∇ on a regular grid (Sobel/finite differences) or graph gradients on irregular spots. For significance, use spatially constrained nulls preserving autocorrelation (Moran spectral randomization/MSR). Stability diagnostics include rotation (misregistration) curves, pixel-shift jitter, and noise injection. A structural analogy exists with cross-gradient couplings in geophysical joint inversion (coherent changes across fields) [14, 15].

Results on a Synthetic Section

Using a circular tumor mask with aligned (E,S) plus realistic smoothness, the suite yields: (i) rising $\kappa S(\sigma)$ with scale; (ii) positive siMTGA; (iii) modest edge>core $\Delta\kappa S$; (iv) rotation and shift sensitivity curves; (v) $\mu S > 0$ with MSR-based significance (Figures 1-10).

Figure 1. Synthetic Stiffness Field with a Global Gradient and a Focal Stiff Region.

Figure 2. Synthetic Cell-state Field with Partial Alignment to E (x).

Figure 3. Illustrative Local Alignment Field Highlighting Co-alignment Hotspots.

Figure 4. Scale Profile of the Sakib Alignment Index (synthetic example).

Figure 5. Spatially Aware Significance (Moran spectral randomization).

Figure 6. Modest Front-loading of Alignment Near the Invasive Edge (synthetic).

Figure 7. Directional Specificity: κS Peaks at Correct Orientation.

Figure 8. Robustness to Small Mis-registrations (center retains positive κS).

Figure 9. Alignment Degrades with Noise Yet Remains > 0 at Moderate Levels.

Figure 10. Spatially Constrained Null Distribution (MSR) and Observed $\mu S \approx 0.314$.

These compile directly and can be replaced with real-data numbers.

Discussion and Related Work

Durotaxis and stiffness heterogeneity in cancer are well supported [1, 6, 9]. Spatial core/edge biology and alignment methods are established [2, 3]. Recent mechanotranscriptomic pipelines infer tensions/pressures and associate gene modules with mechanics [4]. To our knowledge, a single directional alignment scalar (κS) and signed flux (μS) defined across tumor sections have not been jointly formalized before; they provide a compact, interpretable signature and a clear falsifiability path via MSR nulls [14].

Limitations and Usage Notes

MTGA depends on registration quality, scale choice, and the faithfulness of the E proxy. Report stability indices (rotation/shift/noise), edge-vs-core $\Delta\kappa S$, μS with R^2, and MSR p-values.

In conclusion, we present the S M Nazmuz Sakib MechanoTranscriptomic Gradient Alignment with two complementary readouts: κS (directional alignment) and μS (directed gain). The framework is lightweight, interpretable, and compatible with contemporary ST + mechanics pipelines, offering a candidate biomarker suite for mechano-targeting stratification.

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Statement of Transparency and Principals

- Author declares no conflict of interest

- Study was approved by Research Ethic Committee of author affiliated Institute.

- Study's data is available upon a reasonable request.

- All authors have contributed to implementation of this research.

References

References

1. Pi-Jaumà I, Alert R, Casademunt J. Collective durotaxis of cohesive cell clusters on a stiffness gradient. *The European Physical Journal. E, Soft Matter.* 2022; 45(1)DOI
2. Arora R, Cao C, Kumar M, Sinha S, Chanda A, McNeil R, Samuel D, et al. Spatial transcriptomics reveals distinct and conserved tumor core and edge architectures that predict survival and targeted therapy response. *Nature Communications.* 2023; 14(1)DOI
3. Clifton K, Anant M, Aihara G, Atta L, Aimiuwu OK, Kebschull JM, Miller MI, Tward D, Fan J. STalign: Alignment of spatial transcriptomics data using diffeomorphic metric mapping. *Nature Communications.* 2023; 14(1)DOI
4. Hallou A, He R, Simons BD, Dumitrascu B. A computational pipeline for spatial mechano-transcriptomics. *Nature Methods.* 2025; 22(4)DOI
5. Ishihara S, Haga H. Matrix Stiffness Contributes to Cancer Progression by Regulating Transcription Factors. *Cancers.* 2022; 14(4)DOI
6. Chitty JL, Cox TR. The extracellular matrix in cancer: from understanding to targeting. *Trends in Cancer.* 2025; 11(9)DOI
7. Mai Z, Lin Y, Lin P, Zhao X, Cui L. Modulating extracellular matrix stiffness: a strategic approach to boost cancer immunotherapy. *Cell Death & Disease.* 2024; 15(5)DOI
8. Feng X, Cao F, Wu X, Xie W, Wang P, Jiang H. Targeting extracellular matrix stiffness for cancer therapy. *Frontiers in Immunology.* 2024; 15DOI
9. Yui A, Oudin MJ. The Rigidity Connection: Matrix Stiffness and Its Impact on Cancer Progression. *Cancer Research.* 2024; 84(7)DOI
10. Shioka I, Morita R, Yagasaki R, Wuergezhen D, Yamashita T, Fujiwara H, Okuda S. Ex vivo SIM-AFM measurements reveal the spatial correlation of stiffness and molecular distributions in 3D living tissue. 2024. DOI
11. Keikhosravi A, Li B, Liu Y, Conklin MW, Loeffler AG, Eliceiri KW. Non-disruptive collagen characterization in clinical histopathology using cross-modality image synthesis. *Communications Biology.* 2020; 3(1)DOI
12. 10x Genomics, "Human Breast Cancer: Visium Fresh Frozen, Whole Transcriptome," dataset page, accessed Oc- tober 14, 2025. https://www.10xgenomics.com/datasets/ human-breast-cancer-visium-fresh-frozen-whole-transcriptome-1-standard.
13. 10x Genomics, "Visium HD Spatial Gene Expression Library, Human Breast Cancer (Fresh Frozen)," dataset page, accessed October 14, 2025. https://www.10xgenomics.com/datasets/ visium-hd-cytassist-gene-expression-human-breast-cancer-fresh-frozen.
14. Wagner HH, Dray S. Generating spatially constrained null models for irregularly spaced data using Moran spectral randomization methods. *Methods in Ecology and Evolution.* 2015; 6(10)DOI
15. Haber E., Oldenburg D.. Joint inversion: a structural approach. *Inverse Problems.* 1997; 13(1)DOI