

ORAL PRESENTATION FOR RONGHAO'S UNDERGRADUATE RESEARCH

KEYWORDS: RENAL PHYSIOLOGY; TRANSCRIPTOMICS; COMPUTATIONAL NEUROSCIENCE

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Part I

RENAL PHYSIOLOGY

WHY RENAL PHYSIOLOGY AND HYPERTENSION?

SIGNIFICANCE OF PROJECTS

- ▶ Hypertension is the leading cause of health deficiencies.
- ▶ Dietary fructose consumption has increased by **20 times** in 2010 compared to that in 1970.
- ▶ Fructose metabolism in the kidney can affect blood pressure homeostasis and cause hypertension over time.

Table 1. Dietary fructose consumption in the past decades

| Year | Fructose Consumption |
|------|----------------------|
| 1970 | < 2 lbs/person/yr |
| 2010 | > 40 lbs/person/yr |

FRUCTOSE & EXPRESSION OF ALDOSTERONE-RESPONSE GENES

CONTRIBUTION

► **Duration:**

- January 2022 - Present

► **Keywords:**

- Transcriptomics; Epithelial transport in kidney

► **Publication:**

- Submitted an abstract as the first author to the American Physiology Summit

► **Involvement:**

- Designing techniques and approaches
- Multi-disciplinary collaboration
- Sample collection and cataloguing
- Data analysis and interpretation
- Dissemination and presentation of results

FRUCTOSE & EXPRESSION OF ALDOSTERONE-RESPONSE GENES

INTRODUCTION

- ▶ The proximal tubule (PT) reabsorbs fructose via a Na-dependent mechanism [4].
 - SGLT5, *Slc5a10*
- ▶ Reabsorbed fructose increases the epithelial transport in the PT via Angiotensin II-related mechanism [5].
- ▶ Renin Angiotensin Aldosterone System (RAAS)
- ▶ To test the effect of fructose on other segments of the nephrons
 - Aldosterone-Sensitive Distal Tubule (ASDT)
- ▶ **Hypothesis:** *fructose metabolism in PT could affect aldosterone signaling in the distal tubule of rats fed a high-salt diet.*

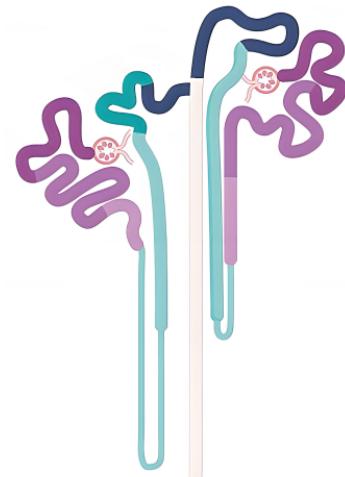
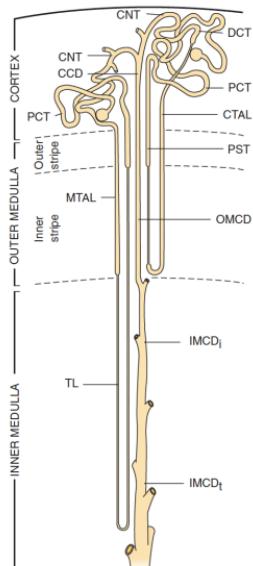


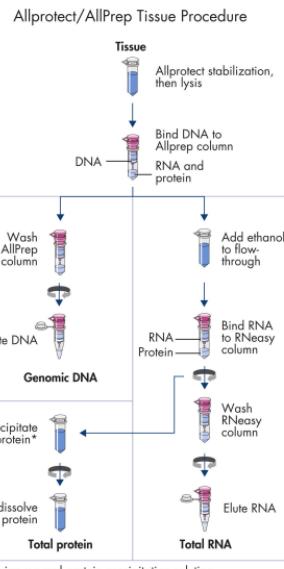
Figure 1. A diagram of superficial and juxtamedullary nephron [8]

FRUCTOSE & EXPRESSION OF ALDOSTERONE-RESPONSE GENES

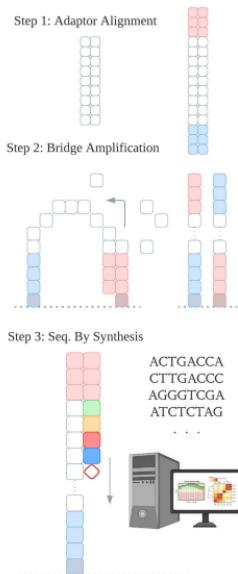
METHODOLOGY: mRNA SAMPLE COLLECTION AND SEQUENCING



(a) Location of PT & ADST [9]



(b) mRNA Purification



(c) Next-Generation Sequencing [1]

Figure 2. The workflow of mRNA data collection and processing

FRUCTOSE & EXPRESSION OF ALDOSTERONE-RESPONSE GENES

METHODOLOGY: SEQUENCE ALIGNMENT

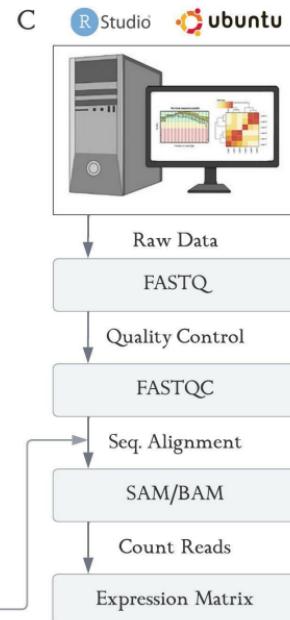
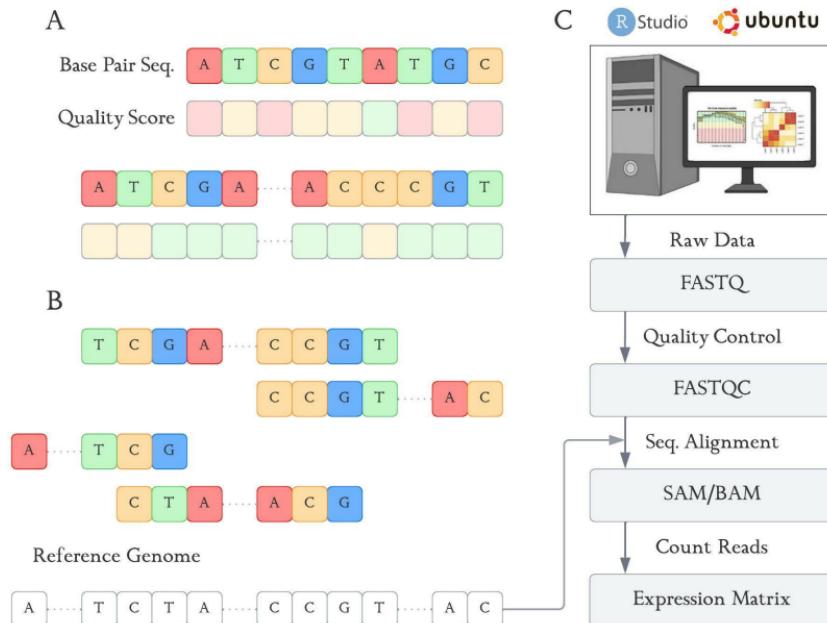


Figure 3. The workflow of Next-Generation Sequencing alignment

(a) Trim the Raw Data (b) Sequence Alignment (c) Processed File Generation

FRUCTOSE & EXPRESSION OF ALDOSTERONE-RESPONSE GENES

METHODOLOGY: MATRIX NORMALIZATION

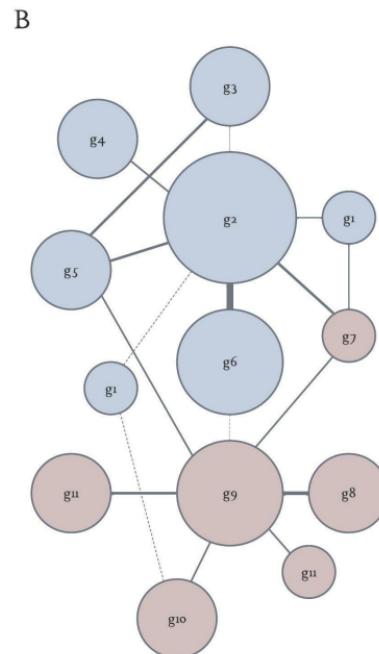
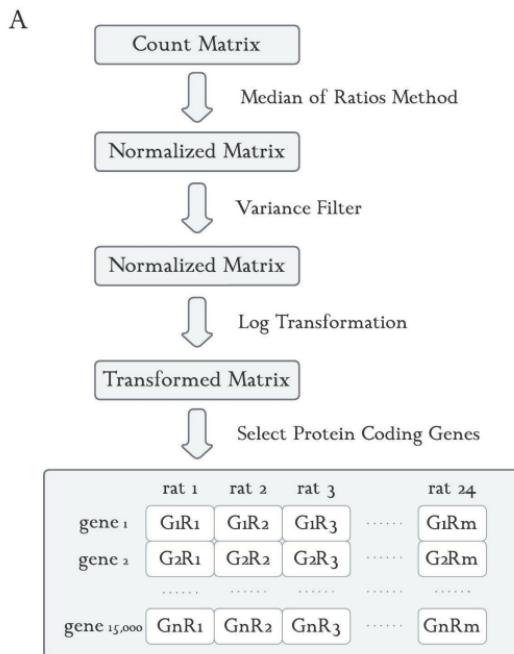


Figure 4. The workflow of matrix data processing (a) Data cleaning (b) Gene Co-expression Network

FRUCTOSE & EXPRESSION OF ALDOSTERONE-RESPONSE GENES

METHODOLOGY: WCGNA I - WEIGHTED CORRELATION MATRIX

- ▶ Weighted Correlation Network Analysis (WGCNA) [6][11]
 - Cluster Similar Genes
- ▶ Co-expression Network
 - Vertex: Gene
 - Edge: Correlation
- ▶ Soft Threshold (Power) Selection
 - Scale-Free Network
 - Scale Independence
 - Connectivity
- ▶ Adjacency Matrix Generation
 - $\text{abs}(\text{cor}(\text{gene1}, \text{gene2}))^{\text{power}}$
 - $(0.5 + \text{cor}(\text{gene1}, \text{gene2}) / 2)^{\text{power}}$

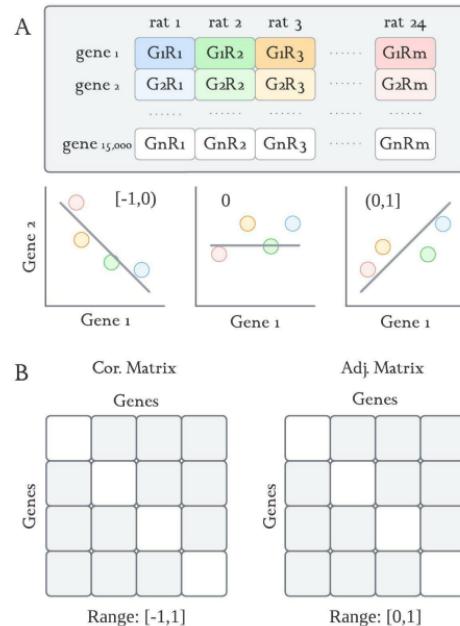


Figure 5. The workflow of WGCNA I (a) Correlation calculation (b) Adjacency matrix generation

FRUCTOSE & EXPRESSION OF ALDOSTERONE-RESPONSE GENES

METHODOLOGY: WCGNA II - MODULE IDENTIFICATION

- ▶ Topological Overlap Measurement (TOM)
 - Measure of Similarity
 - $\uparrow \text{Cor}(i, j) \uparrow \text{TOM}(i, j) \downarrow \text{TOM.dissim}(i, j)$
- ▶ Module Assignment of Genes
 - Hierachical Clustering
 - Gene Dendrogram
- ▶ Module-Trait Relationship
 - Phenotypes, Biological Measurements
 - GO Enrichment analysis

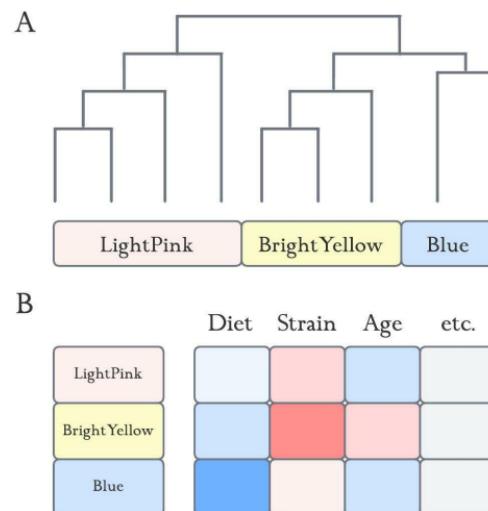


Figure 6. The workflow of WGCNA II (a) Clustering of similar genes (b) Module-Trait Relationship

FRUCTOSE & EXPRESSION OF ALDOSTERONE-RESPONSE GENES

RESULTS: MODULE GENERATION

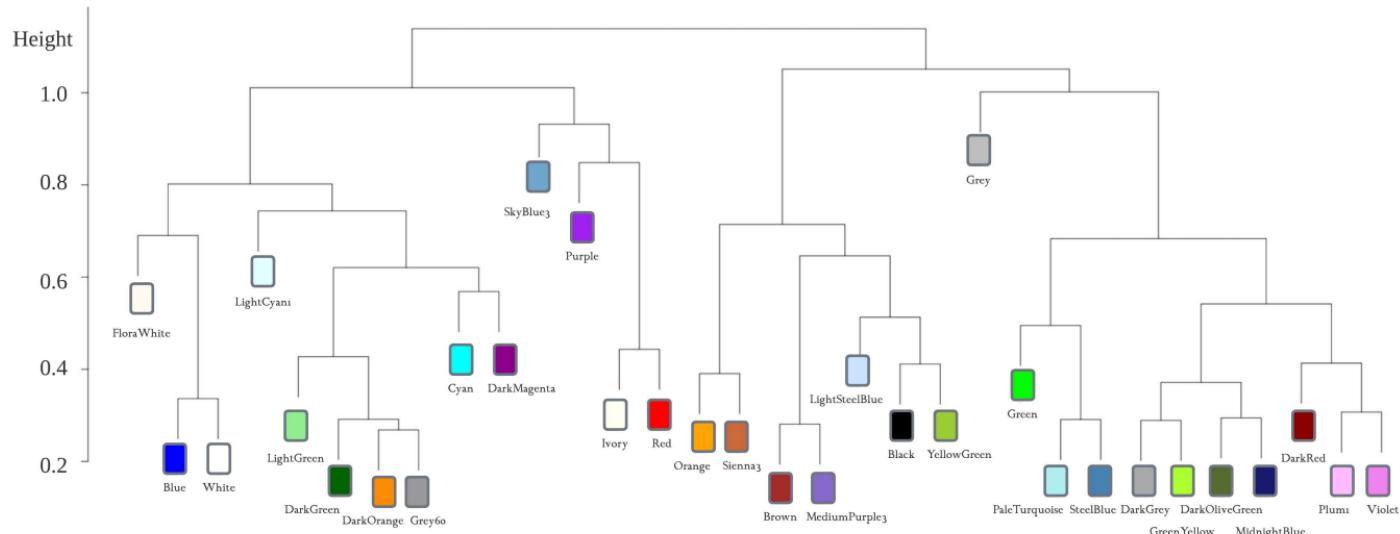


Figure 7. The 32 gene modules generated using WGCNA

FRUCTOSE & EXPRESSION OF ALDOSTERONE-RESPONSE GENES

RESULTS: MODULE TRAIT RELATIONSHIP

► Module Trait Diagram

- correlation index (p-value)
- identify expression changes in response to fructose in both groups

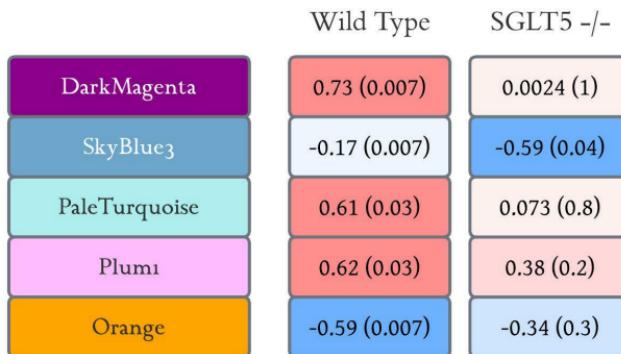


Figure 8. Selected Module-Trait Relationship diagram

FRUCTOSE & EXPRESSION OF ALDOSTERONE-RESPONSE GENES

RESULTS: ALDOSTERONE-RELATED MODULES

- ▶ Open source transcriptome (ASDT epithelial cells) [7]
 - 8619 genes mapped to the rat kidney transcriptome
 - 454 genes significantly changed by Aldosterone
- ▶ Enrichment Analysis
 - 2 modules enriched for aldosterone and correlated with fructose in WT
 - ▶ Paleturquoise ($p < 3 \times 10^{-2}$) & Orange ($p < 4 \times 10^{-2}$)
 - Paleturquoise: Genes involved in Na, Cl and HCO_3^- transport
 - ▶ Scnn1a, ENaC
 - ▶ Slc12a3, NCC
- ▶ **Conclusion:** *On a high-salt diet, kidneys from rats given fructose present higher transcriptional activation of aldosterone-responsive genes than those given glucose.*

FRUCTOSE & EXPRESSION OF ALDOSTERONE-RESPONSE GENES

WORKS TO BE CONTINUED

- ▶ to further explore the transcriptome
- ▶ to identify the specific pathways regulated by aldosterone
- ▶ to conduct quantitative biological experiments if necessary

Part II

COMPUTATIONAL NEUROSCIENCE

WHY COMPUTATIONAL NEUROSCIENCE AND NEURAL ENGINEERING?

SIGNIFICANCE OF PROJECTS

- ▶ A new approach to interact with tools
- ▶ Possibility of rehabilitation after severe impairments and disorders
- ▶ Insights to the brain function and even other subjects

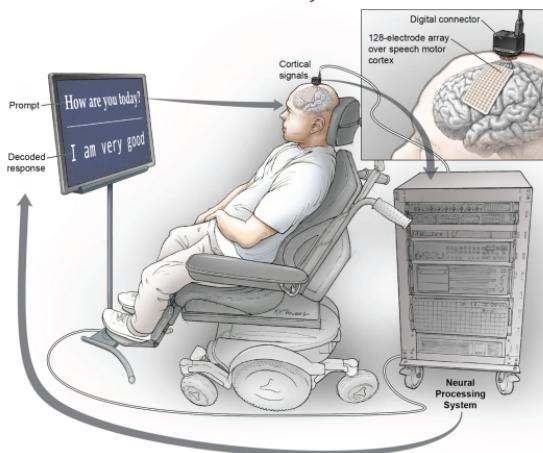


Figure 9. Brain-Computer Interface to restore patients' voice [2]

NEURAL BASIS OF FINGERTIP BIOMECHANICS

CONTRIBUTION

► **Duration:**

- May 2022 - August 2022

► **Keywords:**

- Computational Neuroscience; Tactile Afferent Receptors

► **Publication:**

- Unknown

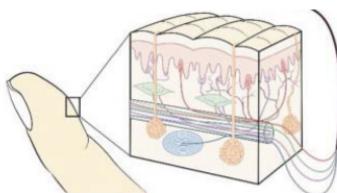
► **Involvement:**

- Data analysis and interpretation
- Dissemination and presentation of results

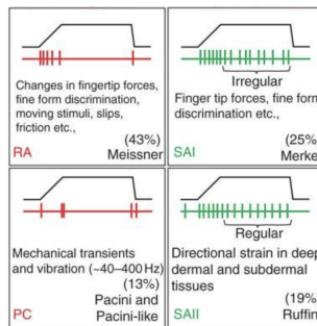
NEURAL BASIS OF FINGERTIP BIOMECHANICS

INTRODUCTION

- ▶ Tactile perception of glabrous skin: 4 Mechanoreceptors
- ▶ What is the effect of Fingertip Biomechanics?
- ▶ What about Fingertip on a compliant texture?



(a) Mechanoreceptor Location [10]



(b) Mechanoreceptor Functions [3]



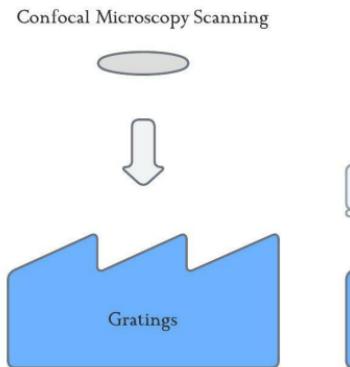
(c) Fabric Pattern of Wool Yarn

Figure 10. Introduction to afferent mechanoreceptors of tactile perception

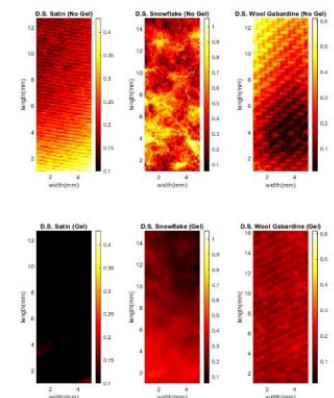
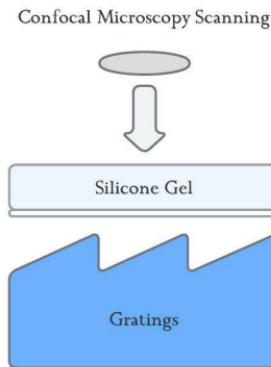
NEURAL BASIS OF FINGERTIP BIOMECHANICS

METHODOLOGY: HEIGHT MAP GENERATION

- ▶ Scanning of raw heights and "skin indentation" for frequency analysis
- ▶ Light refraction and artifacts introduced by scanning



(a) Confocal Microscopy Scanning



(b) Mechanoreceptor Functions

Figure 11. Generation of Height Maps

NEURAL BASIS OF FINGERTIP BIOMECHANICS

METHODOLOGY: ARTIFACT REJECTION I

- ▶ Downsampling
 - Change the resolution of height maps
- ▶ Detrending
 - Flatten the crease and eliminate artifacts
- ▶ Force Normalization
 - Normalize the indentation depth
- ▶ Remaining Problem
 - Scaling Factors & Angle Difference

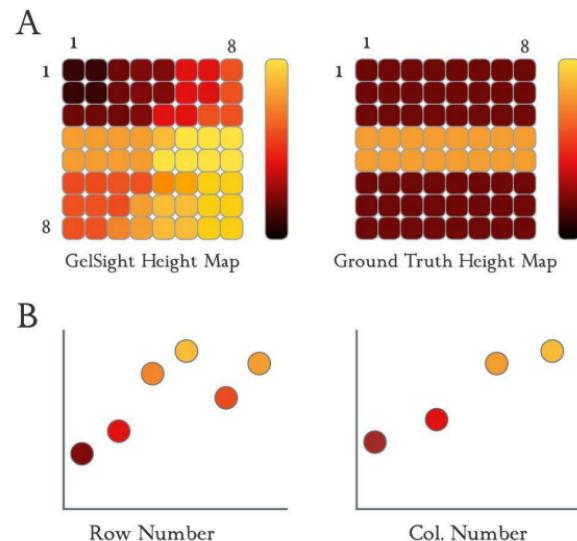


Figure 12. The detrending method (a) Comparison between gelsight and ground truth height map (b) Row-wise and column-wise average height

NEURAL BASIS OF FINGERTIP BIOMECHANICS

METHODOLOGY: ARTIFACT REJECTION II

- ▶ Matlab-embedded image registration
- ▶ Cross Correlation of 2 matrix is given by that

$$\mathbf{C}(k, l) = \sum_{m=0}^{M-1} \sum_{n=0}^{N-1} \mathbf{X}(m, n) \bar{\mathbf{H}}(m - k, n - l)$$

, where $-(P - 1) \leq k \leq M - 1$ and $-(Q - 1) \leq l \leq N - 1$

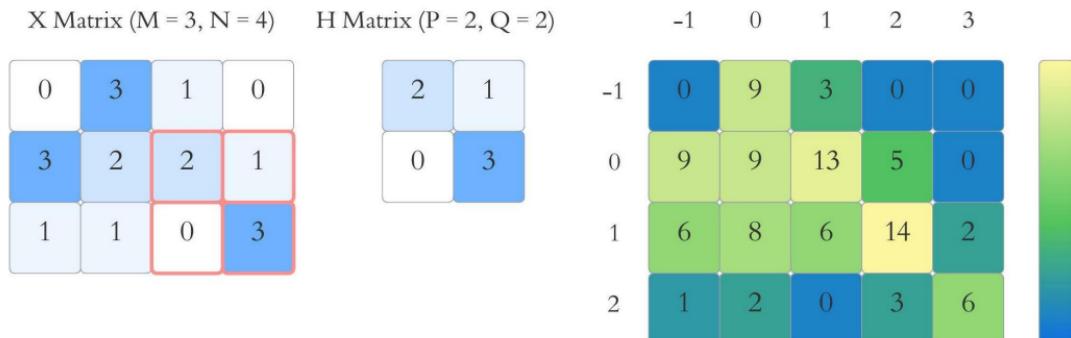
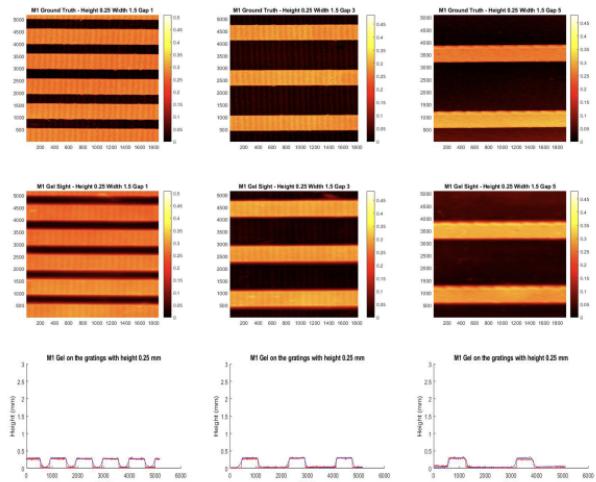


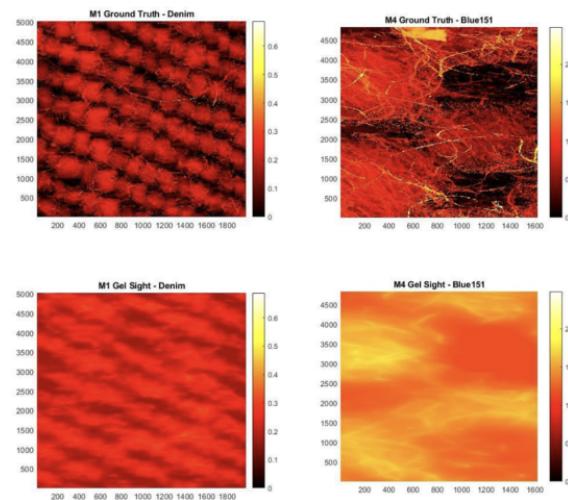
Figure 13. Example of 2-D cross correlation method of 2 matrices

NEURAL BASIS OF FINGERTIP BIOMECHANICS

RESULTS



(a) Aligned Grating Patterns



(b) Aligned Fabric Patterns

Figure 14. Pixel by pixel alignment of compliant and non-compliant textures

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