Nanomechanical Analysis of Renal Tubular Cell Cytoskeleton to Measure Renal Disease

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TARGET 3·4

REDUCE MORTALITY FROM NON-COMMUNICABLE DISEASES AND PROMOTE MENTAL HEALTH

Abstract

This project investigates changes in mechanical properties of kidney cells when exposed to TGF-β1, which is known to induce renal disease [1]. The aim of this project is to provide insight on the progression of diabetic nephropathy from a mechanical perspective based on changes in mechanical properties observed in single cells using atomic force microscopy.

Lists

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   i. subsubitem 1
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Description

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Equations

$$\hat{P}(x \mid G) = \frac{1}{\sigma_G \sqrt{2\pi}} e^{\frac{-1}{2}\left(\frac{x-\mu_G}{\sigma_G}\right)^2} \tag{1}$$

$$\hat{P}(x \mid G) = \phi(x; \mu_G, \sigma_G) \cdot \Phi\left(\alpha_G \cdot \frac{x-\mu_G}{\sigma_G}\right) \tag{2}$$

$$\hat{P}(x \mid G) = \frac{1}{nh} \sum_{i=1}^{n} K\left(\frac{x - x_{i_G}}{h}\right) \tag{3}$$

$\hat{P}(x \mid G)$ :: Group Probability Density Function
x :: Observation (i.e. Young's Modulus)
σ_G :: Group Standard Deviation
μ_G :: Group Mean
$\phi(x; \mu, \sigma)$ :: Normal PDF evaluated at x
α_G :: Group Skew Parameter
$\Phi(z)$ :: Standard Normal CDF
x_{i_G} :: Observed Data Points from Group G
n :: Number of Observations
$K(\cdot)$ :: Kernel Function (i.e. Gaussian)
h :: Bandwidth (Smoothing Parameter)

(4)

Introduction

This project investigates the predictive power of renal tubular epithelial cell stiffness as a biomarker for the progression of Diabetic Nephropathy (DN). DN is a common and serious complication of diabetes resulting in kidney failure due to progressive damage to the nephrons, the functional units of the kidney responsible for filtering the blood [2]. This loss of function is due to physical changes at the cellular level induced by cytokine TGF-β 1 associated with an observable change in cytoskeleton stiffness [3].

A force against indentation curve of a cells can be observed using Atomic Force Microscopy (AFM) where the deflection of a very fine probe on a flexible cantilever is measured to detect contact forces. From the spring constant of the cantilever the indentation and force exerted can be determined as the assembly is advanced into the sample. This curve can then be fitted against an elastic deformation model to determine an apparent Young's Modulus (YM).

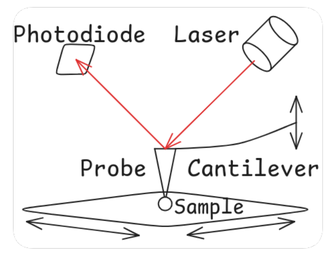
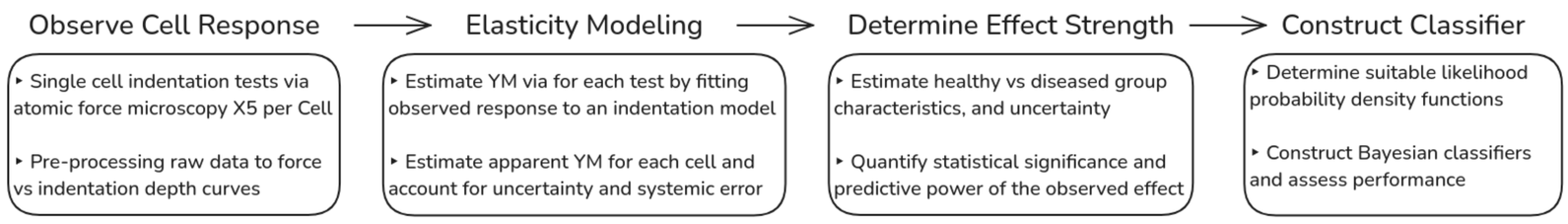


Fig. 1: AFM Diagram

The probability a given cell is healthy or diseased can be predicted from the observed distributions of YM of cells that have not been exposed to TGF-β (Control) and those that have (Treated) by a Bayesian classifier.

Methodology



Figures and Tables

Recommendations

Repeat with larger experimental dataset

Applying the methodology described on larger datasets would allow for a more robust estimate with more extensive testing and validation.

References

[1] M. E. Gentle, S. Shi, I. Daehn, *et al.*, "Epithelial Cell TGF Signaling Induces Acute Tubular Injury and Interstitial Inflammation," *Journal of the American Society of Nephrology : JASN*, vol. 24, no. 5, pp. 787–799, Apr. 30, 2013, ISSN: 1046-6673. DOI: 10.1681/ASN.2012101024. PMID: 23539761. (visited on 02/04/2025).

[2] W. Metcalfe, "How does early chronic kidney disease progress?: A Background Paper prepared for the UK Consensus Conference on Early Chronic Kidney Disease," *Nephrology Dialysis Transplantation*, vol. 22, pp. ix26–ix30, suppl_9 Sep. 1, 2007, ISSN: 0931-0509. DOI: 10.1093/ndt/gfm446. (visited on 01/29/2025).

[3] C. E. Hills, E. Siamantouras, S. W. Smith, P. Cockwell, K.-K. Liu, and P. E. Squires, "TGF modulates cell-to-cell communication in early epithelial-to-mesenchymal transition," *Diabetologia*, vol. 55, no. 3, pp. 812–824, Mar. 1, 2012, ISSN: 1432-0428. DOI: 10.1007/s00125-011-2409-9. (visited on 01/29/2025).