Biophysical Informatics Solutions

Integrated Digital Platform for Characterizing Biological Specimen

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Current Team

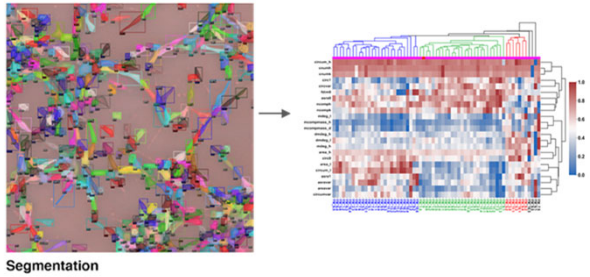
- Michael Mak, PhD, Assistant Professor of Biomedical Engineering, Yale
- Xiangyu Gong, PhD, Postdoctoral Associate, Mak Lab
- Xuchen Zhang, MD, PhD, Associate Professor of Pathology, Yale
- Active collaboration with clinicians who study histopathology samples.
- Mak Research Lab members who are engineering students developing experimental and computational tools to study tissue engineered systems.

About us: The Mak Research Lab specializes in developing advanced tissue engineering systems to model disease processes, performing high resolution imaging and developing image analysis tools to study cell and tissue dynamics, and developing biophysical models. Our research is funded by the NIH (National Institute of General Medical Sciences, National Institute of Biomedical Imaging and Bioengineering, and the National Cancer Institute).

Our Expertise: Interdisciplinary and Integrative Biomedical Engineering

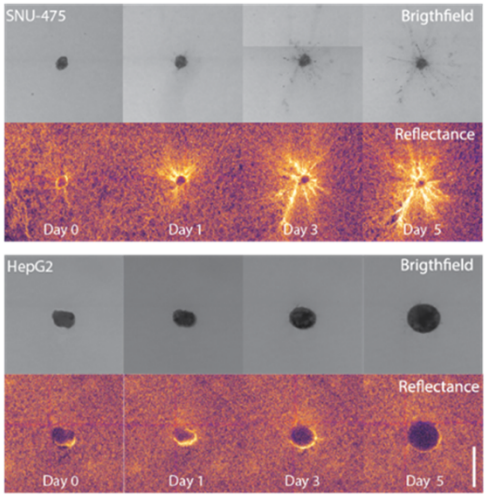
Computational Analytics and Informatics

- extracting complex information from biological imaging data sets



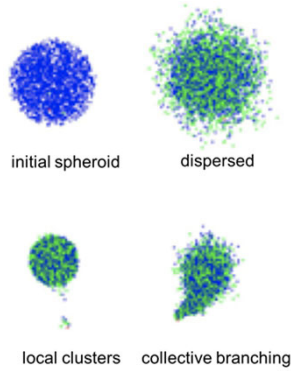
Engineered Tissue Systems to Model Diseases

- patho-physiologically mimicking *tissue models for in vitro studies*



Biophysical Modeling and Theory

- computational modeling based on biophysical principles

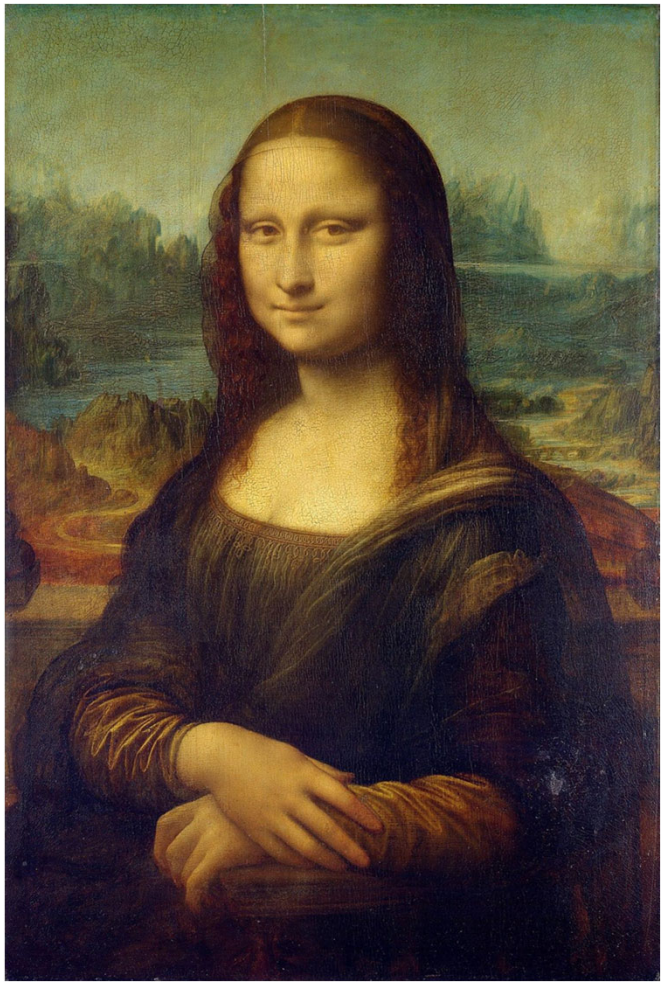


For more information: MakResearchLab.com

Business Opportunity

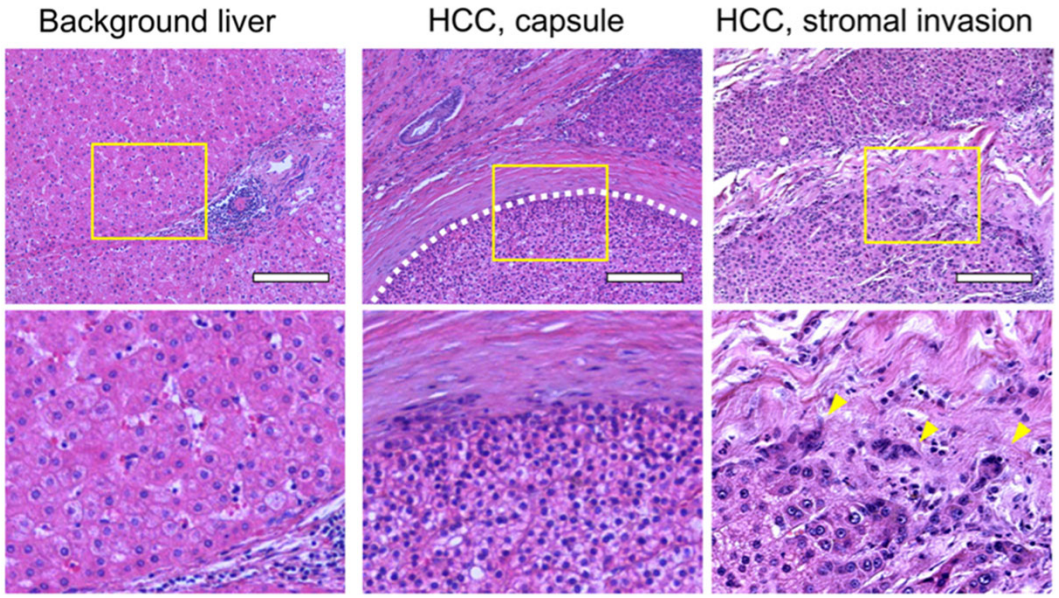
Complexity of Images

- Images contain complex and subtle information.
- They also contain incomplete information.
- Interpreting complex images is challenging.



Biomedical Complexity – Unmet Need

- Biological specimen contains complex information.
- Fixed tissue samples play important roles in disease diagnostics and prognostics.
- Typically, clinical pathologists will manually characterize these samples looking for known patterns, which requires extensive training, is time consuming, and usually highly qualitative.
- **Important medical decisions are made based on assessments of these images.**



Histology Section of Liver Tumor

Challenges and Opportunities

Challenges

- complex data
- manually intensive
- qualitative interpretations
- many data with unknown implications and potential
- incomplete information (static images)

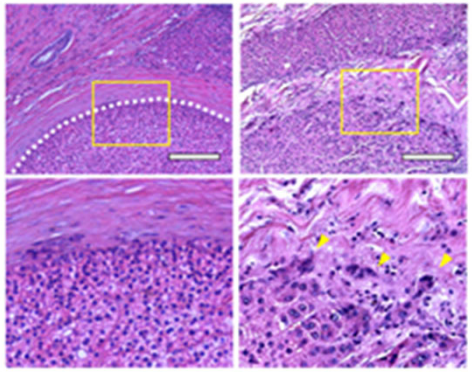
Opportunities

- automation
- detailed, quantitative profiling
- improving unbiased and accurate readouts with decreased time
- uncovering applications for unused data
- augmenting observable data to improve understanding and utility

Our Solution

Inputs

Clinical Tissue Sections



Biophysical Informatics

Outputs

- tissue characterization
- diagnostics, prognostics
- personalized therapy
- and more...

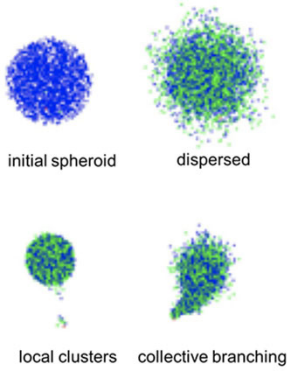
Integrated Digital Platform for Characterizing Biological Specimen

Integrated Digital Platform for Characterizing Biological Specimen

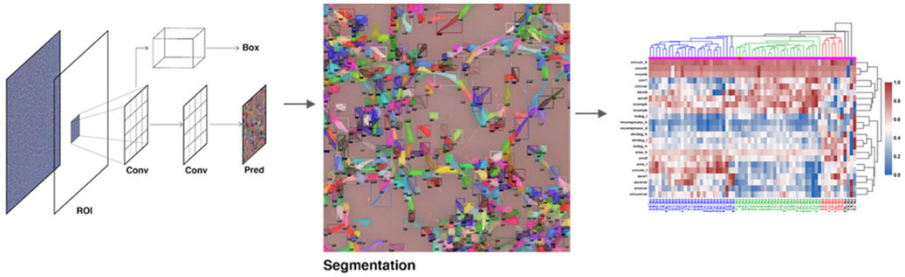
Inside the platform:

Biophysical Informatics

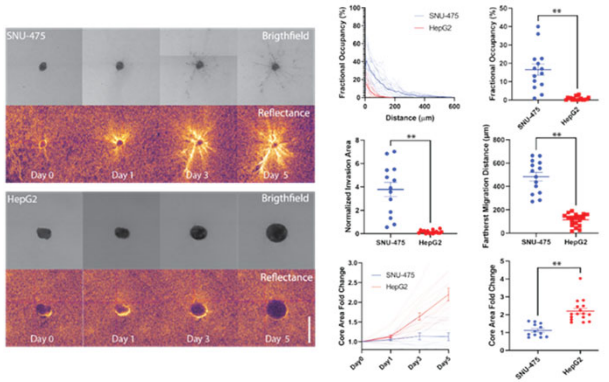
Biophysical theory and models



AI-driven automated data processing and feature extraction.
Biophysical and image-based informatics.



in vitro experiments and database



Summary of how it works

- We take biospecimen, e.g. pathology sections.
- We image and process the images automatically through AI-driven methods.
- We extract complex, quantitative information from the images and perform analytics to characterize profiles observed in the images.
- Patterns from image analytics are connected to our biophysical models and experimental database to generate advanced profiles and mechanistic insights.

- Applications:
  - clinical diagnostics and prognostics
  - personalized therapy guidance
  - improved disease staging and patient stratification
  - biomarker discovery
  - drug development, therapy design

Competition

Computational/AI-based pathology companies

- Philips
- Google
- IBM
- Roche
- Synlab
- PathAI
- Proscia
- Mindpeak.ai

Our Competitive Advantage

Integrated platform – 3-pronged approach:

AI/Automation/Informatics + Experiments + Biophysics

1. AI/Automation/Informatics: Enables automated, rapid, and highly quantitative data characterizations and correlations.
2. Experiments: Growing database of in-house experimental results from advanced engineered tissue systems. Enables temporal and functional information on the behaviors of cells and tissues.
3. Biophysics: Biophysical modeling and theory based on fundamental physical principles of cell-cell and cell-microenvironment interactions.

- Together these provide a comprehensive, mechanistic understanding of clinical samples.

- **Competitors:** Existing computational pathology companies are primarily focused on AI/Informatics approaches, usually lacking in experimental and biophysical modeling/theory support. This leads to mainly correlative speculations. Without the other 2 critical arms, there is a lack of mechanistic understanding and causal decomposition.

Value Creation: 3 Interrelated Channels

- Channel 1: Clinical Pathology
  - Automate clinical pathology sample evaluation.
- Channel 2: Biomarker Discovery
  - Discover novel markers to guide improved diagnostics, prognostics, and optimized+personalized therapy decisions.
- Channel 3: Data-Monetization and Therapeutics
  - Value realization of vast amounts of untapped clinical and biological data.
  - Licensing of data libraries and analytics.
  - Virtualization of medical discoveries.
  - Data-driven novel therapy development.

Value Creation: Channel 1

Channel 1 (near term): Clinical Pathology

- Rationale: There is a growing need for improved pathology services in the US. From 2007-2017, there is a 17% decrease in US pathologists. The decreasing trend of pathologists will likely lead to shortages to the already strained diagnostic system – including delayed and errors in diagnoses. (Metter et al., JAMA Netw Open, 2019)

- Solution: Pathology service for hospitals
  - Automated, quantitative clinical specimen evaluation.
  - Improved workflow efficiency in clinical pathology divisions at hospitals.
  - Improved unbiased and quantitative metrics for diagnostics, prognostics, and patient stratification.
  - Helps counter the shortage of pathologists in the US and globally and improve performance in clinical pathology (accuracy and speed).
- Strategy:
  - Partner with Yale School of Medicine and Yale New Haven Health to integrate into clinical pathology services (Years 1-2).
  - Expand to CT hospitals and then nation-wide (Year 3).
  - 6000+ hospitals in the US. Clinical histology labs process 500+ samples a day. If we charge 1 dollar per sample and process 100,000 samples a year for each hospital, that would translate to 600,000,000 dollars of revenue each year.

Value Creation: Channel 2

Channel 2: Biomarker Discovery

- Rationale: Clinical biomarkers are important signatures that guide our understanding of diseases, can help diagnose and assess therapeutic efficacy, and guide clinical decision making (treatment regimes).
  - There is a limited number of biomarkers for assessing pathology specimen, and large amounts of information in the samples are discarded due to unknown implications. There are significant amounts of untapped information.
- Solution: Data-driven discovery of novel biomarkers
  - Develop new, gold standards for characterizing patient disease status and optimal therapy regimes based on novel biomarker libraries. New standards for evaluating therapeutic efficacy.
  - Personalized therapy based on advanced data profile of each patient.
- Strategy:
  - Our integrated platform enables large scaled, high-content advanced screening of potential biomarkers/patterns for clinical implications. We will apply our platform to characterize new and archived histology sections from clinical pathology labs.
  - Revenue from customized patient profiles and treatment strategies, which will be a % of the total treatment cost. Cancer treatment market alone is estimated to be ~150B, based on various market research reports.

Value Creation: Channel 3

Channel 3: Data Banking and Data Monetization

- Rationale: Large amounts of unused data with untapped potential in clinical specimen.
- Solution: Large-scaled data curation and development of extensive integrated data bank using our platform.
- Strategy:
  - Licensing of data and analytics to pharma and health organizations to improve their platforms and decision making.
  - Licensing proprietary data-driven strategies for therapeutic development.
  - Development of in-house data-driven therapeutics.

Funding

- Blavatnik funds will be utilized to primarily pursue Channel 1. We will first integrate our platform with clinical pathology services at Yale New Haven Health and Yale School of Medicine. Secondary objectives include curation and computer-aided learning of clinical tissue data to help advance Channels 2 and 3.
- Key milestones for the first year: $75-100K
    1. Improve the workflow of clinical pathologists through automation. Test and validate automated computational tools for reproducing evaluations by clinicians. Aim for 90+% accuracy as compared to manual evaluations by clinicians. We will start our work with gastrointestinal (GI) pathologists.
    2. Create a centralized database of 10000+ new clinical samples. We will also curate data from existing open source databases. Apply deep learning methods to understand these data.