# JHU vision lab

# Artificial Intelligence and Machine Learning in Biomedicine and Health Care

#### **René Vidal**

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THE DEPARTMENT OF BIOMEDICAL ENGINEERING





The Whitaker Institute at Johns Hopkins

### Brief History of Artificial Intelligence



MATHEMATICAL INSTITUTE for DATA SCIENCE



# Impact of AI/DL in Computer Vision

• 2012-2014 classification results in ImageNet

2012 Teams %error 2013 Teams %error 2014 Teams Supervision (Toronto) 15.3 Clarifai (NYU spinoff) 11.7 GoogLeNet ISI (Tokyo) 26.1NUS (singapore) 12.9 VGG (Oxford) 26.9 VGG (Oxford) 13.5 Zeiler-Fergus (NYU) **MSRA** 27.0 **XRCE/INRIA** A. Howard 13.5 A. Howard UvA (Amsterdam) 29.6 **OverFeat (NYU)** 14.1 **DeeperVision** 33.4 **INRIA/LEAR** UvA (Amsterdam) 14.2 NUS-BST 15.2 TTIC-ECP Adobe VGG (Oxford) 15.2 XYZ VGG (Oxford) 23.0 UvA

HNS H

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• 2015 results: ResNet under 3.5% error using 150 layers!

Slide from Yann LeCun's CVPR'15 plenary and ICCV'15 tutorial intro by Joan Bruna



CNN non-CNN

%error

6.6

7.3

8.0

8.1

9.5

9.7

10.2

11.2

12.1

### Impact of AI/DL in Speech Recognition



## Impact of AI/DL in Game Playing

• AlphaGo: the first computer program to ever beat a professional player at the game of Go [1]





• Similar deep reinforcement learning strategies developed to play Atari Breakout, Super Mario



Silver et al. Mastering the game of Go with deep neural networks and tree search, Nature 2016 Artificial intelligence learns Mario level in just 34 attempts, <u>https://www.engadget.com/2015/06/17/super-mario-world-self-learning-ai/</u>, <u>https://github.com/aleju/mario-ai</u>



### Potential Impact of AI/DL in Biomedicine





https://www.forbes.com/sites/robertpearl/2018/03/13/artificial-intelligence-in-healthcare/#470c8be1d750



### Potential Impact of AI/DL in Biomedicine

#### Google DeepMind Health



#### **IBM Watson Path**



#### **HEALTH AI MARKET SIZE 2014-2021** \$600M \$6.6B Acquisitions of Al startups are rapidly increasing while the health Al market is 11x set to register an explosive CAGR of 40% through 2021 2014 2021

Source: Accenture analysis



https://www.accenture.com/us-en/insight-artificial-intelligence-healthcare http://medicalfuturist.com/top-artificial-intelligence-companies-in-healthcare/



### What is Biomedical Data Science About?







### Fundamental Challenges: Scale/Modalities





http://ibme.utk.edu/research/



# Fundamental Challenges: Big/Complex Data

- 400 million procedures/year involve at least 1 medical image
- Medical image archives are increasing by 20-40 percent each year
- 1 billion medical images stored in the US (2012)
- 1/3 of global storage is medical image information





at&t



http://www.corp.att.com/healthcare/docs/medical\_imaging\_cloud.pdf



### **Fundamental Challenges: Small Annotations**

- State of the art methods in ML are data hungry
  - Cleaning & annotation of biomedical data is very costly

• State of the art methods in ML are not fully interpretable

- Strong need for
  - Sharing clean, highly annotated data
  - Developing methods that require minimal supervision
  - Developing methods that are interpretable to physicians





## **Our Research in Biomedical Data Science**

### Cellular Level

- Dictionary learning for blood cell detection, classification, counting
- Structured matrix factorization for segmentation of neural activity in calcium imaging
- Metamorphosis for classification of embryonic cardio-myocytes

#### Organ Level

- Compressed sensing and Riemannian geometry for processing diffusion MRI
- Patient/Surgeon Level
  - Assessing surgical skill
  - Assessing children's motions













Ghoreyshi ISBI07; Singaraju CVPR08, CVPR09, TPAMI11; Goh ECCV06, ISBI06, ECCV08, CVPR09; MICCAI09, Neuroimage 12; Cetingul PPMIA09, ISBI09, TBME11, ISBI11, ISBI12, TBME14; Schwab IPMI13; Gorospe MICCAI13, TBME13; Haeffele ICML14; Tao IPCAI12, MICCAI13; Bejar-Zapella MICCAI12, Media13, MICCAI13; Lea: WACV15, ECCV16



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# Machine Learning in Hematology

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### Thermometer











### Hematology Analyzer



umec

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### Machine Learning in Hematology

Complete Blood Count (CBC) using hematology analyzer







$\frown$		Results
WBC		5.65 x 10 <sup>3</sup> cells / µL
RBC	L	3.88 x 10 <sup>6</sup> cells / µL
HGB		13.8 g / dL
HCT		41.3 %
MCV	H	106.5 fL
MCH	н	35.7 pg
MCHC		33.5 g / dL
CHCM		33.3 g / dL
CH		35.2 pg
RDW	н	15.5 %
HDW		2.74 g / dL
PLT	L	87 x 10 <sup>3</sup> cells / µL
MPV		9.4 fL

CBC using lens-free imaging





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lmec

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MPV		9.4 fL





### Computer Vision for Blood Counting & Classification













### Standard Reconstruction of Lens-Free Images



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### Sparse Phase Recovery Reconstruction of Lens-Free Images

 $\min_{X,W,\mu} \frac{1}{2} \| H \odot W - \mu \mathbf{1} - T(z) * X \|_F^2 + \lambda \| X \|_1 \text{ s.t. } |W| = \mathbf{1}$ 







B. Haeffele, R. Stahl, G. Vanmeerbeeck, and R. Vidal, "Efficient Reconstruction of Holographic Lens-Free Images by Sparse Phase Recovery ." MICCAI, 2017.

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### Lens-Free Images of White Blood Cells









### Possible Approach to Detection & Classification



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### **Our Approach to Detection & Classification**

### Method to detect, count and classify cell populations in LFI

- 1. Generative probabilistic model for multi-object detection & classification
- 2. Weakly supervised learning without per-object bounding boxes
- 3. Efficient inference method to detect, count, and classify populations of hundreds to thousands of cells per image



DIAGNOS







### Learning Image Parameters from Purified Blood

- Experimentally isolate cells from a single subclass to obtain purified blood and use detected cells as training examples
- **Domain adaptation challenge**: purified data may not be representative mixed-cell populations

DIAGNOS











Mean Absolute Error	CNN	CSC	Ours
Granulocytes - normal	27.8	31.1	4.5
Lymphocytes - normal	12.8	9.5	4.6
Monocytes - normal	15.9	21.9	4.7
Granulocytes - all	28.6	30.1	6.8
Lymphocytes - all	11.6	8.3	5.6
Monocytes - all	18.9	22.3	5.5

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# Machine Learning in Neuroscience

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### **Single Electrode**



Functional MRI

### **Electrode Arrays**



- Classical gold standard
- One neuron at a time
- Whole brain activity
- Averaged over 1000s of neurons
- Multiple neurons simultaneously
- Limited spatial information



- Fluorescent microscopy technique
  - Optical recording of brain activity
  - Neurons "flash" when active electrically



• Video can be approximated as the sum of rank-1 matrices





- Desired properties of shape and spike matrices
  - U<sub>i</sub> should be sparse (low L1)
  - U<sub>i</sub> should be compact (low TV)
  - V<sub>i</sub> should be sparse (low L1)

 $Y \approx \sum U_i V_i^\top D$ 



Haeffele, Young, Vidal. Structured Low-Rank Matrix Factorization: Optimality, Algorithm, and Applications to Image Processing, ICML '14





#### **Raw Data**

#### Sparse

+ Low Rank

#### + Total Variation



Haeffele, Young, Vidal. Structured Low-Rank Matrix Factorization: Optimality, Algorithm, and Applications to Image Processing, ICML '14



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## Machine Learning in Regenerative Medicine

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### Machine Learning in Regenerative Medicine

- Cardiovascular disease is the world's leading cause of death.
  - 17.3 million deaths per year.
  - 787,000 in the US (2011).
- Myocardial infarction is one of the leading causes of sudden cardiac arrest.
- Stem cells present a potential avenue to treating myocardial infarction.



https://www.heart.org/



http://www.georgeinstitute.org/units/cardiovascular



Laflamme, Chen, Naumova, Muskheli, Fugate, Dupras, Reinecke, Xu, Hassanipour, Police, O'Sullivan, Collins, Chen, Minami, Gill, Ueno, Yuan, Gold, Murray. Cardiomyocytes derived from human embryonic stem cells in prosurvival factors enhance function of infarcted rat hearts. Nature biotechnology 25(9):1015–24, 2007



### Machine Learning in Regenerative Medicine

- Predict cell phenotype from the shape of its action potential
- Maturation process affects the shape of the action potential





Gorospe, Zhu, Milrod, Zambidis, Tung, Vidal. Automated grouping of action potentials of human embryonic stem cell-derived cardiomyocytes. TBME13. Gorospe, Younes, Tung, Vidal. A metamorphosis distance for embryonic cardiac action potential

Gorospe, Zhu, He, Tung, Younes, Vidal. Efficient metamorphosis computation for classifying

embryonic cardiac action potentials. MICCAI15.



### Machine Learning in Regenerative Medicine

• **Metamorphosis** interpolation produces intermediate shapes that better resemble those of a cardiac action potential.



$$d_{\mathcal{M}}^{2}(I_{0}, I_{1}) = \inf_{\substack{v, I \\ I(t, 0) = I_{0}(t) \\ I(t, 1) = I_{1}(t)}} \int_{0}^{1} \frac{1}{2} \left( \|v(t, \tau)\|_{V}^{2} + \frac{1}{\sigma^{2}} \left\| \frac{\partial I}{\partial \tau}(t, \tau) + \frac{\partial I}{\partial t}(t, \tau) v(t, \tau) \right\|_{L^{2}}^{2} \right) d\tau$$



Gorospe, Zhu, Milrod, Zambidis, Tung, Vidal. Automated grouping of action potentials of human embryonic stem cell-derived cardiomyocytes. TBME14. Gorospe, Younes, Tung, Vidal. A metamorphosis distance for embryonic cardiac action potential interpolation and classification. MICCAI13.

Gorospe, Zhu, He, Tung, Younes, Vidal. Efficient metamorphosis computation for classifying embryonic cardiac action potentials. MICCAI15.



### **Clustering Embryonic CM Action Potentials**

• Clustering results for 9 cell clusters of 6940 embryonic APs





Gorospe, Zhu, Milrod, Zambidis, Tung, Vidal. Automated grouping of action potentials of human embryonic stem cell-derived cardiomyocytes. TBME14. Gorospe, Younes, Tung, Vidal. A metamorphosis distance for embryonic cardiac action potential interpolation and classification. MICCA113. Gorospe, Zhu, He, Tung, Younes, Vidal. Efficient metamorphosis computation for classifying embryonic cardiac action potentials. MICCA115.



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## Machine Learning in Brain Image Analysis

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- The human brain contains 100 billion neurons connected in a complex network of fiber bundles.
- Studies show that in neurological disorders such as schizophrenia, autism and Alzheimer's disease, these connections are damaged.
- By mapping brain connections, we can compare neuro anatomies of healthy and diseased brains to develop new tools for diagnosis of neurological diseases.









### Finding biomarkers of neurological disease in diffusion MRI data



**JOHNS HOPKINS** MATHEMATICAL INSTITUTE for DATA SCIENCE angular resolution diffusion images and its applications to ODF-based morphometry" ECCV06, ECCV08, CVPR09, MICCAI09, Neuroimage11. Cetingul et al. "Group action induced averaging for HARDI processing" ISBI12, ISBI12, TBME14 Schwab et al. "Rotation invariant features for HARDI" MICCAI12,

IPMI13, CDMRI15

### Reconstruction of dMRI images





- **Problem**: dMRI currently too slow for clinical use (requires 100s of MRIs)
- **Question**: How can we accelerate acquisition but still estimate accurate fiber tracks?
- Solution: Compressed Sensing





E Schwab, R Vidal, N Charon. (k, q)-Compressed Sensing for dMRI with Joint Spatial-Angular Sparsity Prior, arXiv 2017 E Schwab, R Vidal, N Charon. Efficient Global Spatial-Angular Sparse Coding for Diffusion MRI with Separable Dictionaries, arXiv 2016 E Schwab, R Vidal, N Charon, Spatial-Angular Sparse Coding for HARDI. MICCAI 2017



- High throughput neuroinformatics: bits of neuroscience at 1mm scale
  - 3000 brains
  - 1000x1000x500x100 dimensions
  - 1000-2000 relevant variables
- BrainGPS generates a machine learnable feature vector, a BRAINPRINT.







Brain Science Institute, Johns Hopkins University Michael Miller, Susumu Mori, Andreia Faria, Kenichi Oishi

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# Machine Learning in Surgery

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## Machine Learning in Surgery

• RMIS has the potential to revolutionize our understanding of modeling, teaching and evaluating human manipulation skills.



Modeling the skills of human expert surgeons to train a new generation of students. (more)

• The goal of the project is to develop quantitative methods for modeling surgical tasks and evaluation of surgical skill.





### Machine Learning in Surgery

Recognizing surgical gestures and assessing the skill level of a surgeon in kinematic and video data of a surgical procedure





Bejar, Zappella, Vidal. Surgical Gesture Classification from Video Data, MICCAI12 (Best paper Award) Zappella, Bejar, Hager, Vidal. Surgical Gesture Classification from Kinematic and Video Data, MedIA13

Tao, Zappella, Hager, Vidal. Surgical Gesture Segmentation and Recognition, MICCAI13

Tao, Elhamifar, Khudanpur, Hager, Vidal. Sparse HMMs for Surgical Gesture



### Modeling the Language of Surgery

- Similar to speech, surgical motion is not random:
  - A procedure is composed of tasks (incision, suturing, knot tying, etc.)
  - A task is composed of gestures (insert needle, pull needle, etc.)
  - Procedures, tasks and gestures follow a grammar.



 Our goal: de surgical grar

Reiley, C.E., Lin, H.C., Varadarajan, B., Vagolgyi, B., Khudanpur, S., Yuh, D.D., Hager, G.D.: Automatic recognition of surgical motions using statistical modeling for capturing variability. In: Medicine Meets Virtual Reality. (2008) 396–401



### Markov/Semi-Markov Random Field Models



- Inference: find sequence of gestures using a modified Viterbi
- Learning: find parameters using structural output SVMs

Bejar, Zappella, Vidal. Surgical Gesture Classification from Video Data, MICCAI12 (Best paper Award)
Zappella, Bejar, Hager, Vidal. Surgical Gesture Classification from Kinematic and Video Data, MedIA13
Tao, Zappella, Hager, Vidal. Surgical Gesture Segmentation and Recognition, MICCAI13
Tao, Zappella, Hager, Vidal. Surgical Gesture Segmentation and Recognition, MICCAI13
Tao, Elhamifar, Khudanpur, Hager, Vidal. Sparse HMMs for Surgical Gesture Classification and Skill Evaluation, IPCAI12
Sefati, Cowan, Vidal. Learning Shared, Discriminative Dictionaries for Surgical Gesture Segmentation and Classification, M2CAI15
Lea, Hager, Vidal. An improved model for segmentation and recognition of fine-grained activities with application to surgical training tasks, WACV15



### Segmental Spatio-Temporal CNNs



C. Lea, A. Reiter, R. Vidal, G. Hager. Segmental Spatiotemporal CNNs for Fine-grained Action Segmentation. ECCV 2016

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### **Encoder-Decoder Temporal Conv Nets**



C. Lea, M. Flynn, R. Vidal, A. Reiter, G. Hager. Temporal Convolutional Networks for Action Segmentation and Detection. CVPR 2017

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### Accuracy of Surgical Gesture Segmentation



for DATA SCIENCE



	Model	Accuracy	Edit			Model	Accuracy	Edit
Sensors	LC-SC-CRF	81.9*	78.4*		Sensors	LC-SC-CRF	81.8	58.5
	s-st-cnn	79.2	82.6			s-st-cnn	82.1	55.5
	ED-TCN	82.4	89.3			T-CNN	84.8	76.9
Video	LC-SC-CRF	-	-			lc-sc-crf	-	_
	s-st-cnn	74.2	66.6		Video	s-st-cnn	72.0	62.0
	ED-TCN	78.3	85.6			ED-TCN	71.0*	62.0*

C. Lea, G. Hager, R. Vidal. An improved model for segmentation and recognition of fine-grained activities with application to surgical training

JOHNS HOPKINSC. Lea, A. Reiter, R. Vidal, A. Reiter, G. Hager. Temporal Convolutional Networks for Action Segmentation and Detection. CVPR 2017 MATHEMATICAL INSTITUTE



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# Machine Learning in Rehabilitation Therapy

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## Machine Learning in Rehabilitation Therapy

### Pediatric rehabilitation based on human-robot interaction







Effrosyni Mavroudi, Lingling Tao, Rene Vidal, Deep Moving Poselets for Video Based Action Recognition, WACV 2017 Lingling Tao and Rene Vidal, Moving Poselets: A Discriminative and Interpretable Skeletal Motion Representation for Action Recognition, ICCVW 2015



### Summary

### Cellular Level

- Dictionary learning for blood cell detection, classification, counting
- Structured matrix factorization for segmentation of neural activity in calcium imaging
- Metamorphosis for classification of embryonic cardio-myocytes

### Organ Level

- Compressed sensing and Riemannian geometry for processing diffusion MRI
- Patient/Surgeon Level
  - Assessing surgical skill
  - Assessing children's motions













Ghoreyshi ISBI07; Singaraju CVPR08, CVPR09, TPAMI11; Goh ECCV06, ISBI06, ECCV08, CVPR09; MICCAI09, Neuroimage 12; Cetingul PPMIA09, ISBI09, TBME11, ISBI11, ISBI12, TBME14; Schwab IPMI13; Gorospe MICCAI13, TBME13; Haeffele ICML14; Tao IPCAI12, MICCAI13; Bejar-Zapella MICCAI12, Media13, MICCAI13; Lea: WACV15, ECCV16



### Mathematical Institute for Data Science (MINDS)

- Establish fundamental principles behind the analysis and interpretation of massive amounts of complex high-dimensional data
- We are creating new
  - Masters
  - PhD
- We are hiring
  - Faculty
  - Postdocs
  - Students



















https:// People

























https://www.minds.jhu.edu/people/

### More Information,

### Vision Lab @ Johns Hopkins University http://www.vision.jhu.edu

Center for Imaging Science @ Johns Hopkins University http://www.cis.jhu.edu

Johns Hopkins Mathematical Institute for Data Science <u>http://www.minds.jhu.edu</u>





