Artificial Intelligence in Medicine

Wei-Hung Weng, MD, MMSc

UP-MIT-Stanford-AeHIN Big Data for Health Conference and Workshops for Asia-Pacific

July 4, 2017

Disclosure

- No conflict of interest

Brief History

- Rule-based
- Mimicking human decision making process
- Human curated features

- MYCIN expert system (Stanford)
- INTERNIST-1 (U Pittsburg)

MYCIN

```
--------PATIENT-1--------
1)  Patient's name: (first-last)
**  FRED SMITH
2)  Sex:
**  MALE
3)  Age:
** 55
4)  Have you been able to obtain positive cultures from a site
    at which Fred Smith has an infection?
**  YES
  --------INFECTION-1--------
  5)  What is the infection?
  **  PRIMARY-BACTEREMIA
  6)  Please give the date and approximate time when signs or symptoms
      of the primary-bacteremia (INFECTION-1) first appeared. (mo/da/yr)
  **  MAY 5, 1975
  The most recent positive culture associated with the
  primary-bacteremia (INFECTION-1) will be referred to as:
    --------CULTURE-1--------
    7)  From what site was the specimen for CULTURE-1 taken?
    ** BLODD
    = BLOOD
    8)  Please give the date and time when this blood culture
        (CULTURE-1) was obtained. (mo/da/yr)
    ** MAY 9, 1975
    The first significant organism from this blood culture
    (CULTURE-1) will be referred to as:
      --------ORGANISM-1--------
      9)  Enter the identity of ORGANISM-1:
      **  UNKNOWN
            {typically the identity is not known and must be inferred}
      10)  Is ORGANISM-1 a rod or coccus (etc.):
      **  ROD
      11)  The gram stain of ORGANISM-1:
      **  GRAMNEG
      12)  Did ORGANISM-1 grow aerobically?
      **  YES (.8)
```

Szolovits, Artificial Intelligence in Medicine 1982

```
My therapy recommendation will be based on the following probable
  infection(s) and potential causative organism(s):
INFECTION-1 is PRIMARY-BACTEREMIA                    {possible identities}
<Item 1> The identity of ORGANISM-1 may be PSEUDOMONAS-AERUGINOSA
<Item 2> The identity of ORGANISM-1 may be KLEBSIELLA-PNEUMONIAE
<Item 3> The identity of ORGANISM-1 may be E.COLI
<Item 4> The identity of ORGANISM-1 may be BACTEROIDES-FRAGILIS
<Item 5> The identity of ORGANISM-1 may be ENTEROBACTER
<Item B> The identity of ORGANISM-1 may be PROTEUS-NON-MIRABILIS

  46)  On a scale of 0 to 4, where higher numbers indicate increasing
       severity how would you rate Fred Smith's degree of sickness?
  **  3
  47)  Does Fred Smith have a clinically significant allergic
       reaction to any antimicrobial agent?
  **  NO
  48)  Fred Smith's weight in kilograms (or <number> POUNDS):
  **  70
                          {note that 2 drugs cover for 6 potential organisms)
[Rec 1] My preferred therapy recommendation is as follows:
  In order to cover for Items <1 2 3 5 6>:
    Give:  GENTAMICIN
    Dose:  119 mg (1.7 mg/kg) q8h IV [or IM] for 10 days
    Comments:  Modify dose in renal failure
  In order to cover for Item <4>:
    Give:  CLINDAMYCIN
    Dose:  595 mg (8.5 mg/kg) q6h IV [or IM] for 14 days
    Comments:  If diarrhea or other GI symptoms develop, patient
      should be evaluated for possible pseudomembranous colitis.

Do you wish to see the next choice therapy?
**  Y                                    {alternative choices are available}
Which, If any, of the above drugs do you wish eliminated from
  consideration?
**  CLINDAMYCIN
[Rec 2] Next best therapy recommendation:
  In order to cover for Items <2 3 4 5 6>:
    Give:  CHLORAMPHENICOL
```

MYCIN

Szolovits, Artificial Intelligence in Medicine 1982

MYCIN

(a) **** HOW DID YOU DECIDE THAT ORGANISM-1 MIGHT BE AN E.COLI?**
I used RULE021 to conclude that the identity of ORGANISM-1 is
e.coli. This gave a cumulative CF of (.47).
Then I used RULE084 to conclude that the identity of ORGANISM-1
is e.coli. This gave a cumulative CF of (.55).
Finally, I used RULE003 to conclude that the identity of
ORGANISM-1 is e.coli. This gave a cumulative CF of (.74).

(b) **** DID YOU USE RULE 163 TO FIND OUT ANYTHING ABOUT ORGANISM-1?**
RULE163 was tried in the context of ORGANISM-1, but it failed
because it is not true that the patient has had a
genito-urinary tract manipulative procedure (clause 3).

(c) **** DID RULE 116 TELL YOU ANYTHING ABOUT INFECTION-1?**
No. RULE116 would be relevant to the primary-bacteremia when
applied to ORGANISM-1.
But clause 2 ("the gram stain of the organism is not known")
was already known to be false for ORGANISM-1, so the rule
was never tried.

(d) **** WHY DIDN'T YOU CONSIDER STREPTOCOCCUS AS A POSSIBILITY FOR ORGANISM-1?**
The following rule could have been used to determine that the
identity of ORGANISM-1 was streptococcus: RULE033
But clause 2 ("the morphology of the organism is coccus")
was already known to be false for ORGANISM-1, so the rule
was never tried

Szolovits, Artificial Intelligence in Medicine 1982

INTERNIST-I

```
ABDOMEN GUARDING INVOLUNTARY LOCALIZED ?
NO

Please Enter Findings of TRANSFUSION <S> HX
*GO

TRANSFUSION <S> MULTIPLE HX 7
NO

DISREGARDING: SKIN SPIDER ANGIOMATA, CREATININE BLOOD INCREASED,
UREA NITROGEN BLOOD 60 TO 100

CONSIDERING: FECES LIGHT COLORED, JAUNDICE, LIVER ENLARGED
SLIGHT, ALKALINE PHOSPHATASE BLOOD GTR THAN 2 TIMES NORMAL, SGOT
GTR THAN 400, WBC GTR THAN 30000, SGPT 200 TO 600

PURSUING: HEPATIC LEPTOSPIROSIS
CONCLUDE: HEPATIC LEPTOSPIROSIS

DISREGARDING: SKIN SPIDER ANGIOMATA, UREA NITROGEN BLOOD 60 TO 100

CONSIDERING: OLIGURIA HX, CREATININE BLOOD INCREASED

RULEOUT: RENAL LEPTOSPIROSIS, GLOMERULONEPHRITIS ADVANCED CHRONIC,
LEAD NEPHROPATHY, GLOMERULONEPHRITIS ACUTE, PYELONEPHRITIS
CHRONIC, DIABETIC NEPHROPATHY
```

Szolovits, Artificial Intelligence in Medicine 1982

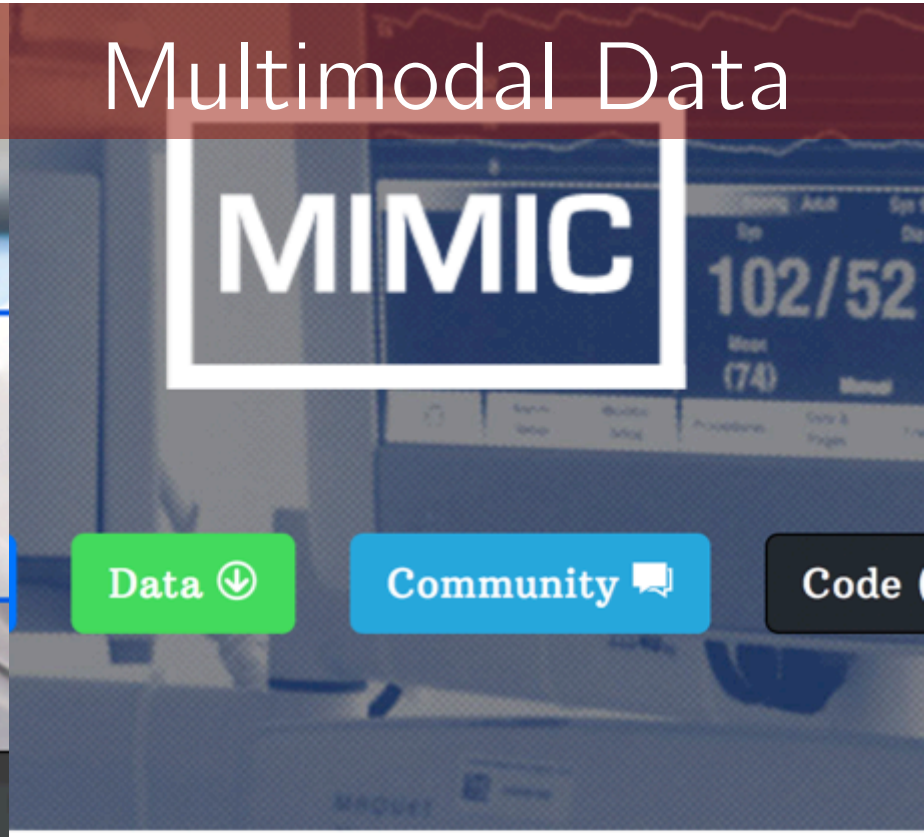
Problems

- Poor generalization due to clinical uncertainty
- Could not fit into clinical workflow

Now?

- Rule-based → Data-driven
- Dealing with uncertainty
- Why?

Multimodal Data

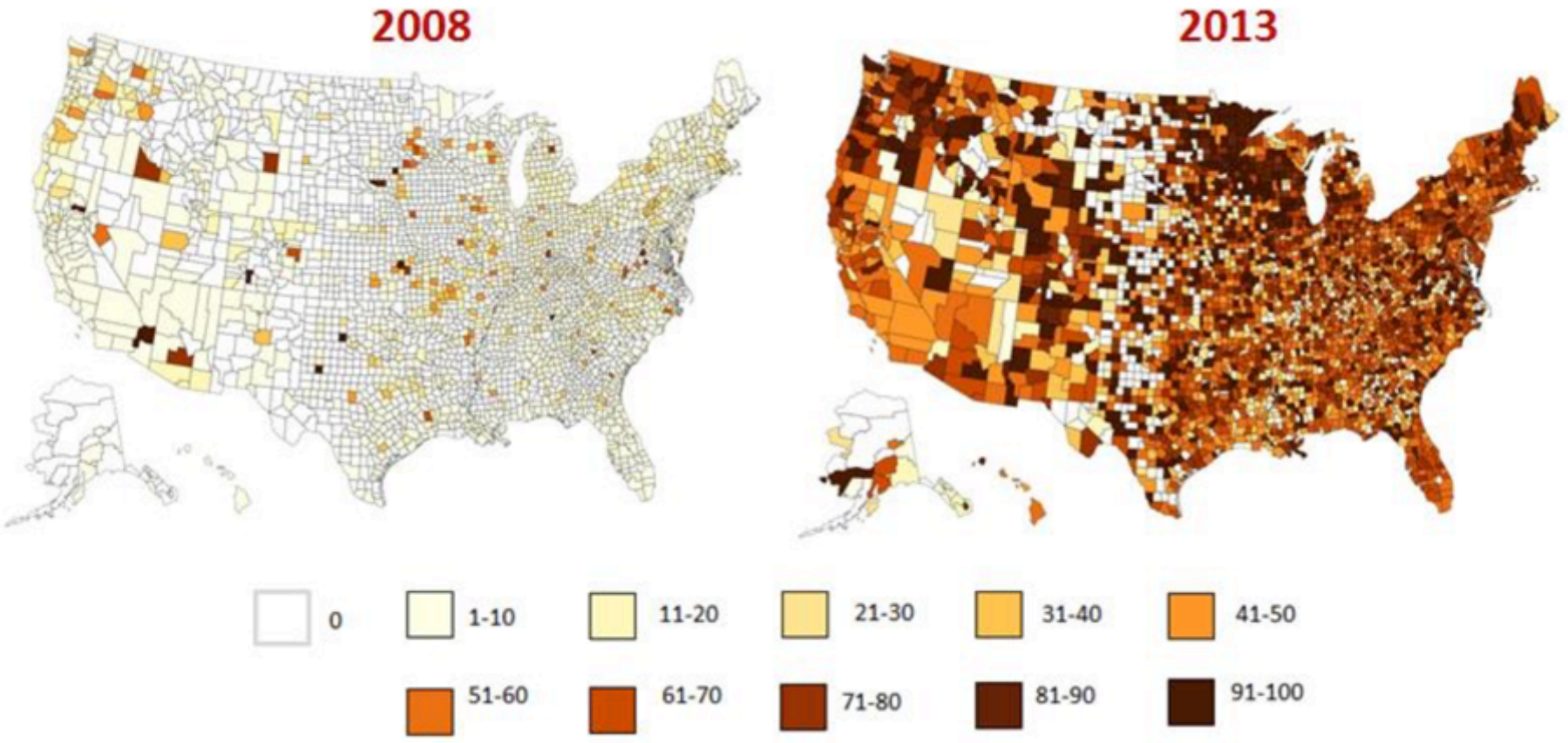


e MIMIC data or code in your work, please cite the follow
publication:

III, a freely accessible critical care database. Johnson AE
Shen L, Lehman L, Feng M, Ghassemi M, Moody B, Szolo
d Mark RG. Scientific Data (2016). DOI: 10.1038/sdata.20
lable from: http://www.nature.com/articles/sdata201635

https://mimic.physionet.org/
http://eicu-crd.mit.edu/

Adoption of EHR



Courtesy by Owen Hsu (Wistron)

Standardization

Water Sports category

1st: Hit or struck by falling object due to accident to canoe or kayak – V9135XA

2nd: Civilian watercraft involved in water transport accident with military watercraft – V94810

3rd: Burn due to water-skis on fire – V9107XA

Strange Places category

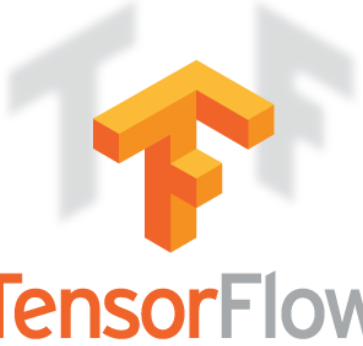
01 Hurt at the library
Y92241

02 Hurt at swimming pool of prison as the place of occurrence
Y92146

03 [illegible]
Y92253

https://www.linkedin.com/pulse/most-bizarre-icd-10-codes-infographic-nina-keller

Democratization of Knowledge and Resources



Why Now?

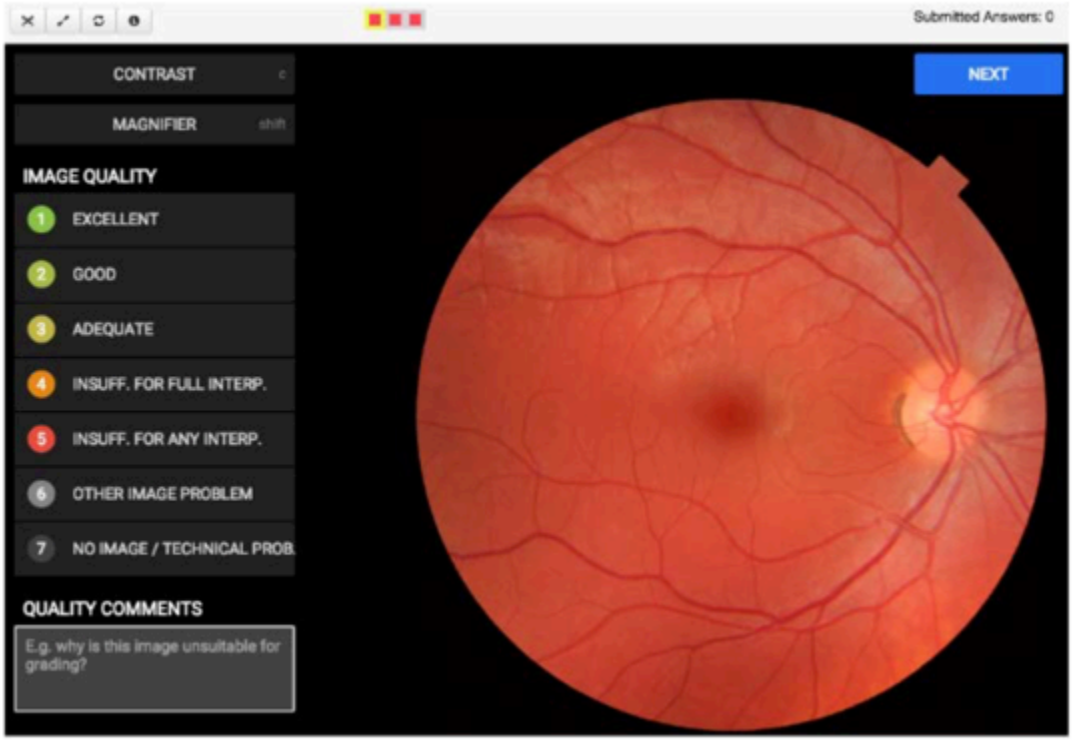
- High quality (?) multimodal data
  - Variety, volume, velocity
  - Social media, sensor, wearable, vital signs, lab data, notes, imaging, -omics
  - Adoption of EHR
- Standardization
- Advances and democratization in ML
  - Open-source / algorithms & tools
  - Different approaches of knowledge representation

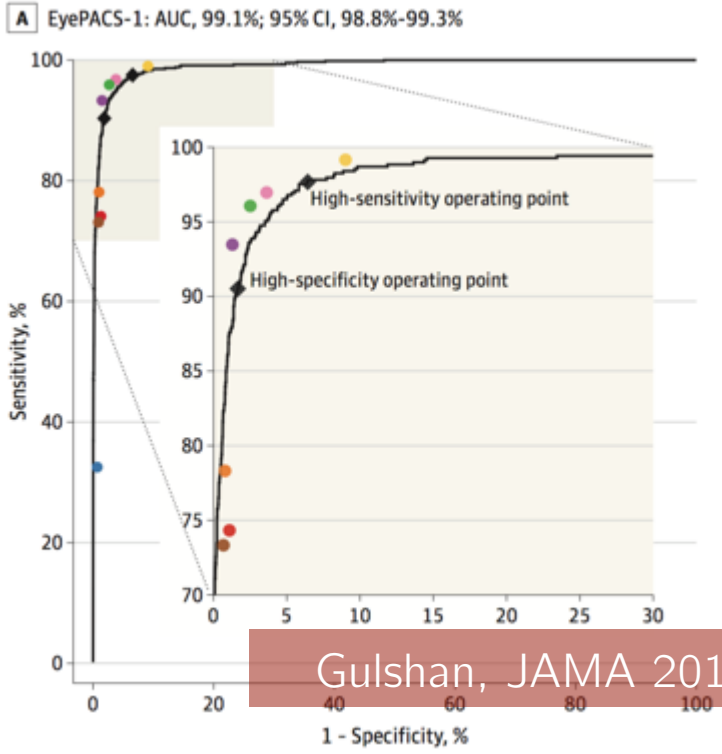
Medical Imaging

JAMA | Original Investigation | INNOVATIONS IN HEALTH CARE DELIVERY

Development and Validation of a Deep Learning Algorithm for Detection of Diabetic Retinopathy in Retinal Fundus Photographs

Varun Gulshan, PhD; Lily Peng, MD, PhD; Marc Coram, PhD; Martin C. Stumpe, PhD; Derek Wu, BS; Arunachalam Narayanaswamy, PhD; Subhashini Venugopalan, MS; Kasumi Widner, MS; Tom Madams, MEng; Jorge Cuadros, OD, PhD; Ramasamy Kim, OD, DNB; Rajiv Raman, MS, DNB; Philip C. Nelson, BS; Jessica L. Mega, MD, MPH; Dale R. Webster, PhD



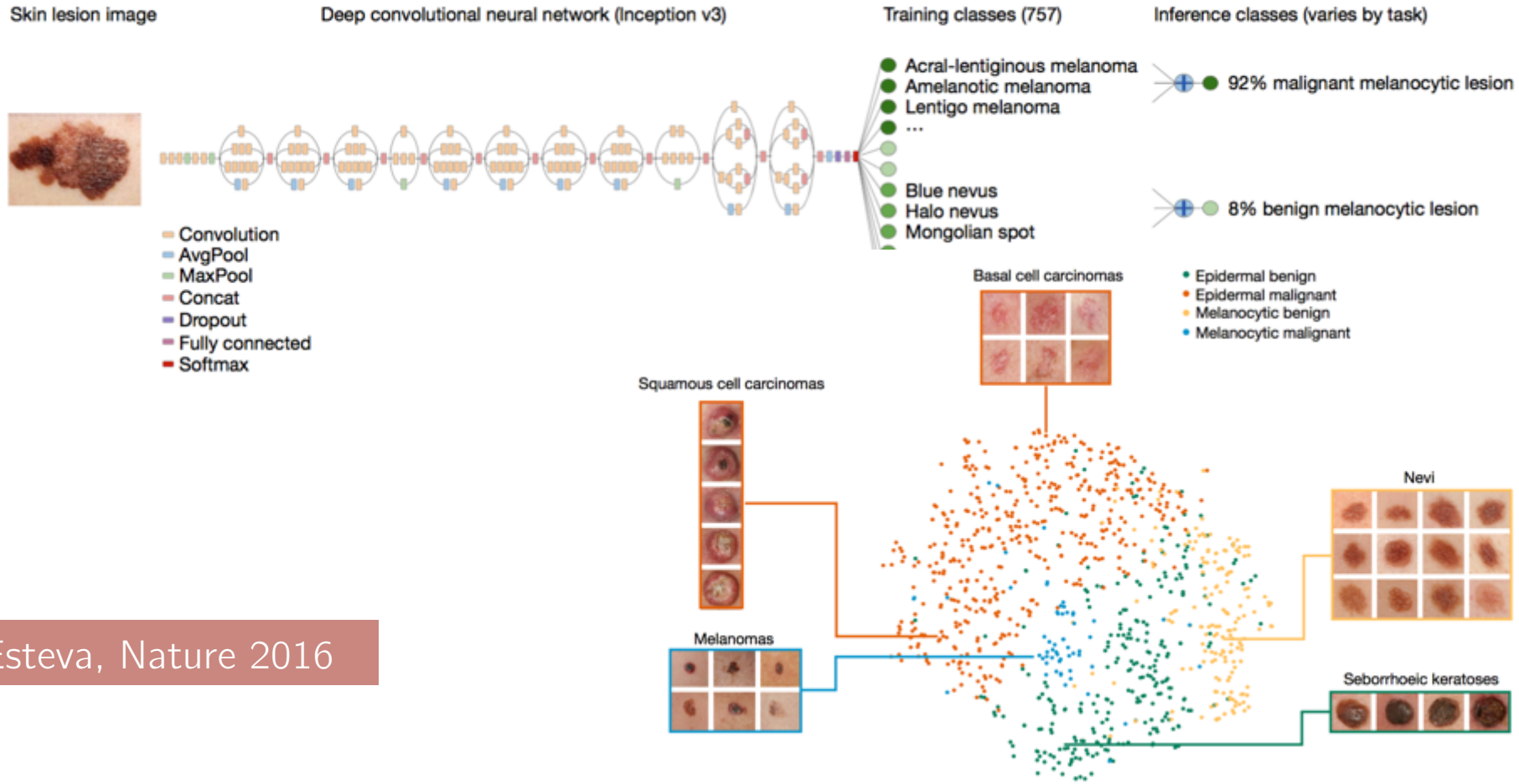


Gulshan, JAMA 2016

Medical Imaging

Dermatologist-level classification of skin cancer with deep neural networks

Andre Esteva[1]*, Brett Kuprel[1]*, Roberto A. Novoa[2,3], Justin Ko[2], Susan M. Swetter[2,4], Helen M. Blau[5] & Sebastian Thrun[6]



Esteva, Nature 2016

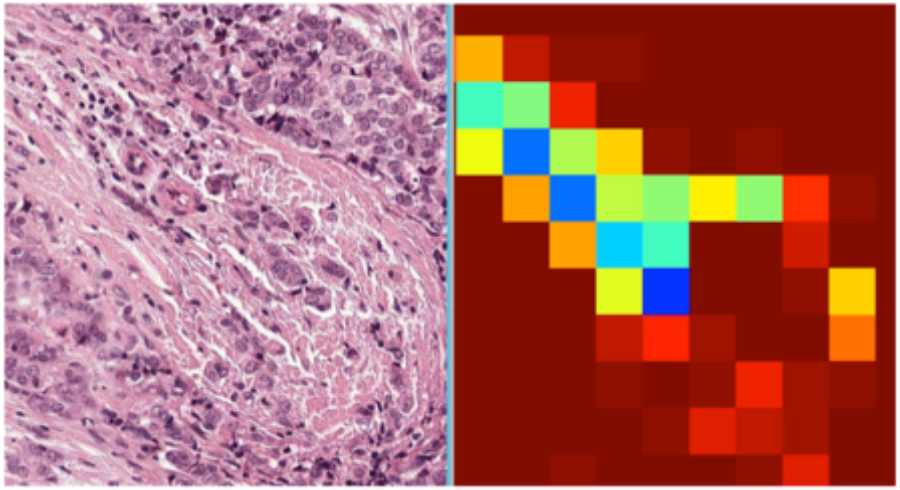
Medical Imaging

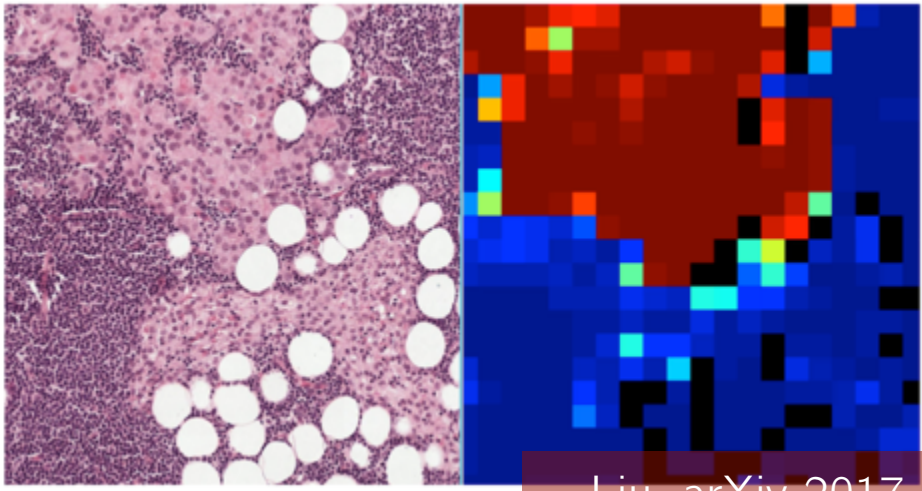
Detecting Cancer Metastases on Gigapixel Pathology Images

Yun Liu[1*], Krishna Gadepalli[1], Mohammad Norouzi[1], George E. Dahl[1], Timo Kohlberger[1], Aleksey Boyko[1], Subhashini Venugopalan[2**], Aleksei Timofeev[2], Philip Q. Nelson[2], Greg S. Corrado[1], Jason D. Hipp[3], Lily Peng[1], and Martin C. Stumpe[1]

{liuyun,mnorouzi,gdahl,lhpeng,mstumpe}@google.com

[1]Google Brain, [2]Google Inc, [3]Verily Life Sciences, Mountain View, CA, USA





Liu, arXiv 2017

Medical Text

Using Machine Learning to Parse Breast Pathology Reports

Adam Yala,[1] Regina Barzilay,[1] Laura Salama,[3] Molly Griffin,[2] Grace Sollender,[8] Aditya Bardia,[10] Constance Lehman,[5] Julliette M. Buckley,[2] Suzanne B. Coopey,[2] Fernanda Polubriaginof,[9] Judy E. Garber,[6] Barbara L. Smith,[2] Michele A. Gadd,[2] Michelle C. Specht,[2] Thomas M. Gudewicz,[4] Anthony Guidi,[7] Alphonse Taghian,[3] and Kevin S. Hughes[2]

Pathology Report: REMOVED_ACCESSION_ID
ACCESSIONED ON: REMOVED_DATE
CLINICAL DATA: Carcinoma **right breast**.
*** FINAL DIAGNOSIS ***
LYMPH NODE (SENTINEL), EXCISION
(REMOVED_CASE_ID): METASTATIC CARCINOMA IN 1 OF 1 LYMPH NODE.
NOTE: The metastatic deposit spans 0.19cm and is identified on H&E and cytokeratin immunostains. A second cytokeratin-positive but cauterized focus likely also represents metastatic tumor (<0.1cm). There is **no evidence of extranodal extension**. BREAST (RIGHT), EXCISIONAL BIOPSY
(REMOVED_ACCESSION_ID : REMOVED_CASE_ID -B):
INVASIVE DUCTAL CARCINOMA (SEE TABLE #1). **DUCTAL CARCINOMA IN-SITU**, GRADE 1. **ATYPICAL DUCTAL HYPERPLASIA**. **LOBULAR NEOPLASIA (ATYPICAL LOBULAR HYPERPLASIA)**.
TABLE OF PATHOLOGICAL FINDINGS #1 INVASIVE CARCINOMA
Tumor size: Cannot evaluate. Grade: 1.
Lymphatic vessel invasion: Not identified.
Blood vessel invasion: Not identified.
Margin of invasive carcinoma: Invasive carcinoma extends to less than 0.2cm from the inferior margin of the specimen.
Stains for receptors: Outside **immunohistochemical stains demonstrate that the tumor cells express estrogen and progesterone receptors.**

Name	Extraction
Breast Side	Right
Ductal Carcinoma in Situ	Present
Invasive Lobular Carcinoma	Absent
Invasive Ductal Carcinoma	Present
Cancer	Present
Lobular Carcinoma in Situ	Absent
Atypical Ductal Hyperplasia	Present
Atypical Lobular Hyperplasia	Present
Lobular Neoplasia	Present
Flat Epithelial Atypia	Absent
Blunt Adenosis	Absent
Atypia	Present
Positive Lymph Nodes	Present
Extracapsular Axillary Nodal Extension	Absent
Isolated Cancer Cells in Lymph Nodes	Absent
Lymphovascular Invasion	Absent
Blood Vessel Invasion	Absent
Estrogen Receptor Status	Positive
Progesterone Receptor Status	Positive
HER 2 (FISH) Status	Unknown

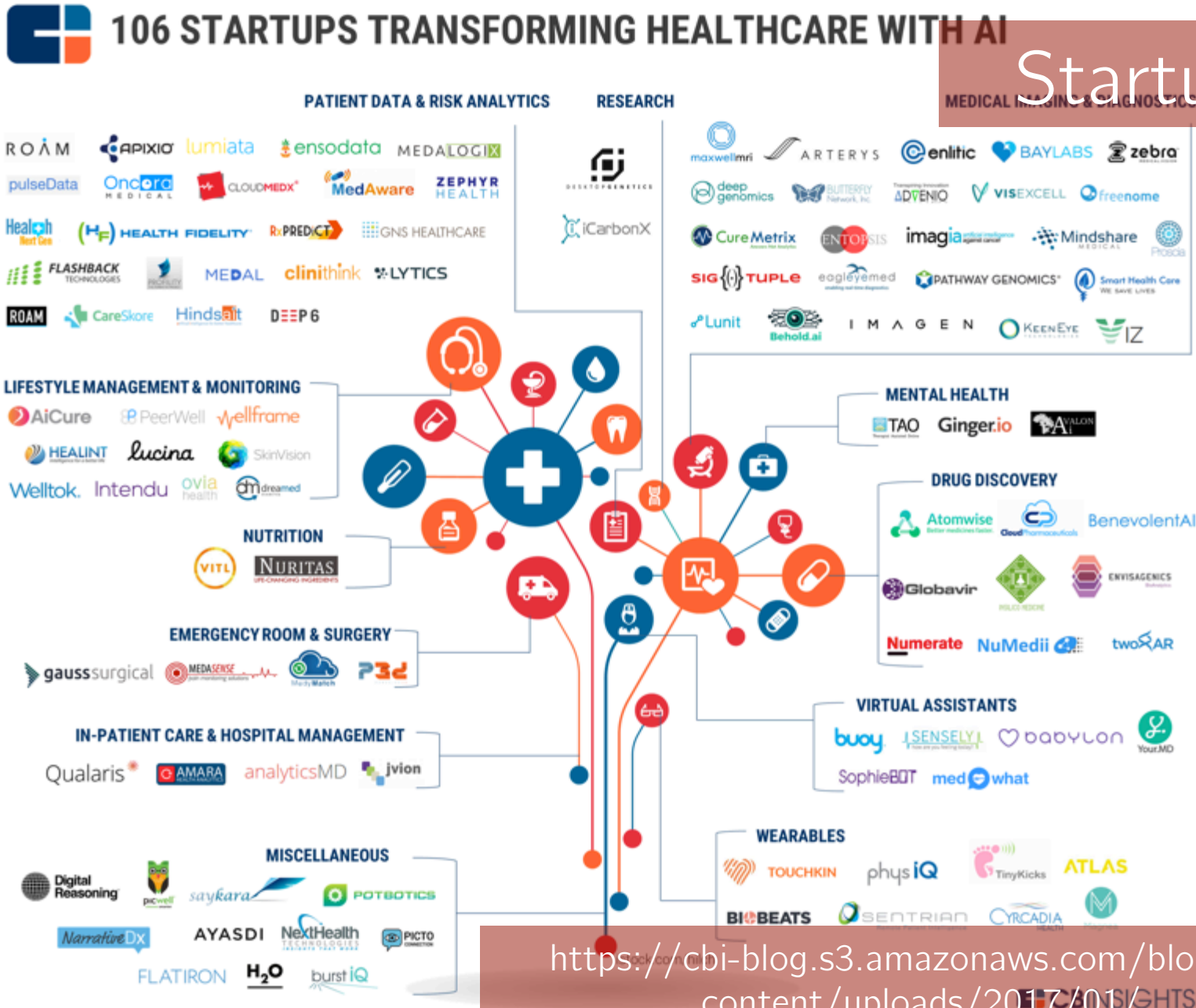
Category	Accuracy	F-score
Breast side	1.0	1.0
DCIS	.99	.99
ILC	.99	.99
IDC	1.0	1.0
Carcinoma	.94	.94
LCIS	1.0	.98
ADH	.90	.90
ALH	.98	.98
Lobular Neoplasia	.97	.97
Flat Epithelial Atypia	1.0	1.0
Blunt Adenosis	1.0	1.0
Atypia	.91	.91
Positive LN	.98	.98
ECE	.97	.97
ITC in LN	.96	.96
LVI	.92	.88
BVI	.93	.90
ER Status	.97	.96
PR Status	.97	.95
HER 2 Status	.96	.94
Report-Level	.90	N/A
Average	.97	.96

Yala, arXiv 2016

Achievement in Industry

- Watson
  - Identify pulmonary embolism on CT
  - Detect abnormal wall motion on echocardiography
  - Watson Oncology in Japan, India, ...
- Enlitic
  - Fracture detection on radiographs
- DeepMind Health
  - NHS collaboration
- Lumiata
- ...

Startups



https://cbi-blog.s3.amazonaws.com/blog/wp-content/uploads/2017/01/healthcare_AI_map_2016_1.png

Clinical Perspective

- Precision / Personalized medicine
  - For
    - Oncology
    - Rare diseases
    - Mental disorders
  - Applications
    - Drug discovery
    - Outcome prediction
      - Lifespan prediction
      - Disease progression
    - Chronic disease management
      - Early prediction of blood glucose for self-management

CS/AI/ML Perspective

- Risk stratification
- Causal inference
- Bias
- Time-series
- Unstructured data
- Interpretability
- Disease progression modeling
- Reasoning and decision making

Issues

- Privacy / Data security
  - Open-source and ubiquitous
  - Innovation, ecosystem
- Data quality
- Transparency
- Domain specific vs. generalization

Replacing Your Job?

The world's first artificially intelligent lawyer was just hired at a law firm

Chris Weller

May 16, 2016, 10:26 AM 44,723

FACEBOOK LINKEDIN TWITTER EMAIL PRINT

Lawyers can get a bad reputation for being slimy and conniving, but ROSS has neither of those qualities.

Ask ROSS to look up an obscure court ruling from 13 years ago, and ROSS will not only search for

http://www.businessinsider.com/the-worlds-first-artificially-intelligent-lawyer-gets-hired-2016-5

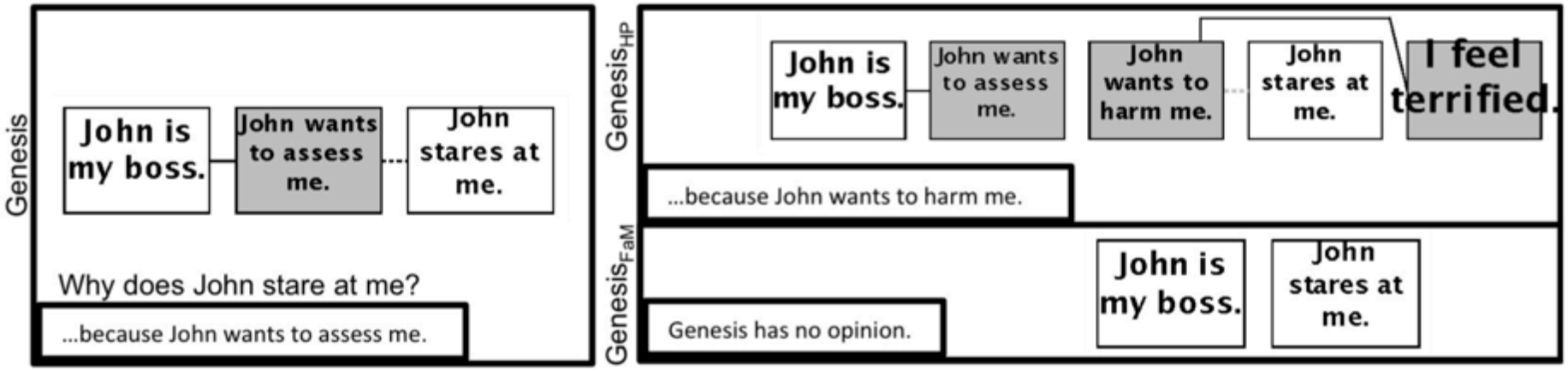
Limitations of AI

- Computational intelligence $\neq$ computational consciousness
- Procedure
- Emotion
- Thinking, reasoning and decision making
  - Inference
  - Abstraction
  - Cognition
  - Commonsense knowledge
  - Insight

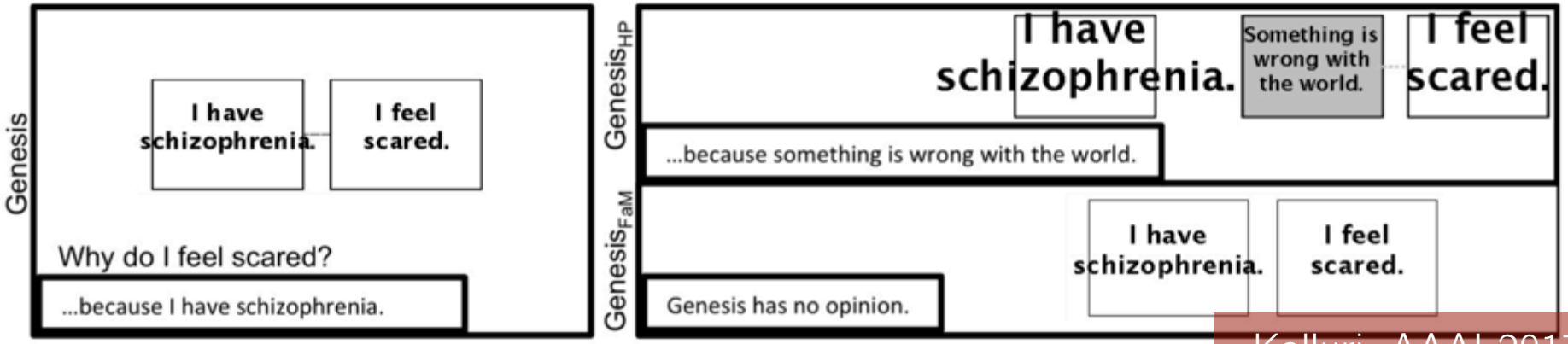
Inducing Schizophrenia in an Artificially Intelligent Story-Understanding System

Pratyusha Kalluri and Patrick Henry Winston

(B) System performance on the Paranoid Delusion Task



(C) System performance on the Persistence of Delusion Task

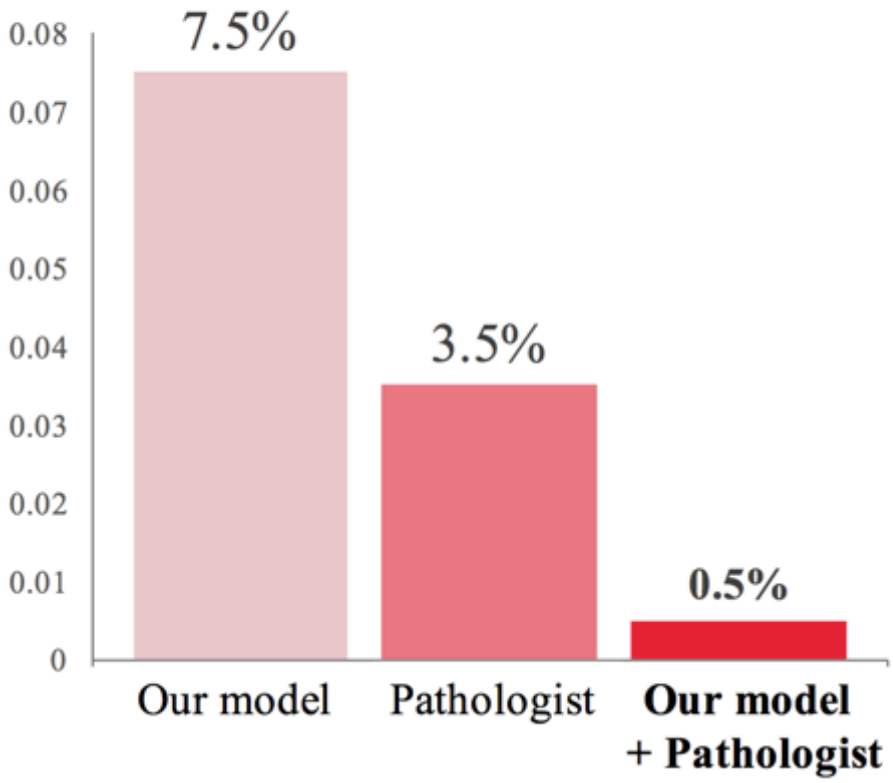


Kalluri, AAAI 2017

What We Can Do

- Find good problems, collect reliable data
- Collaboration > Expert or AI only
  - Expert: high-level integration, interpretation and decision making (learn Bayesian logic, statistics, and data science and be aware of other sources of information!)
  - AI: pattern recognition and massive repetitive tasks
- Share
  - AI researchers open-source platforms and algorithms
  - You can open-source data and knowledge
  - We can do nothing without sharing!
- Experience
  - Learning from AI
  - Communicating with AI

Deep Learning vs Pathologist



The **combination** of a pathologist and the Beck Lab deep learning system **reduces error rate** by 85% **to 0.5%.**

Courtesy by Dr. Andrew Beck (PathAI)

VIEWPOINT

INNOVATIONS IN HEALTH CARE DELIVERY

Adapting to Artificial Intelligence
Radiologists and Pathologists as Information Specialists

Saurabh Jha, MBBS, MRCS, MS
Department of Radiology, University of Pennsylvania, Philadelphia.

Eric J. Topol, MD
Scripps Research Institute, La Jolla, California.

Artificial intelligence—the mimicking of human cognition by computers—was once a fable in science fiction but is becoming reality in medicine. The combination of big data and artificial intelligence, referred to by some as the fourth industrial revolution,[1] will change radiology and pathology along with other medical specialties. Although reports of radiologists and pathologists being replaced by computers seem exaggerated,[2] these specialties must plan strategically for a future in which artificial intelligence is part of the health care workforce.

Radiologists have always revered machines and tech-

This progress in imaging has c
radiologists. Radiology, once confin
ages, such as chest radiographs, has
plex and data rich. Cross-sectional
and magnetic resonance, by sho
greater clarity, has made diagnosis
stances; for example, a ruptured an
a chest radiograph but actually seen
has come at a price—the amount o
markedly. For example, a radiolo
4000 images in a CT scan of multi

Jha, JAMA 2016

Take Home Message

- Problems and reliable data source > Big data and algorithms
- AI is part of the healthcare workforce
- Human-machine collaboration
- Share your data and knowledge
- Learn from AI, communicate with AI

- Acknowledgement
  - Leo Celi (MIT), Mornin Feng (NUS), Alvin Marcelo (UP-AeHIN)
  - Peter Szolovits (MIT), David Sontag (MIT)

- ckbjimmy@mit.edu
- Wei-Hung Weng (LinkedIn)

- http://ckbjimmy.github.io/2017_cebu