

UC San Diego
SCHOOL OF MEDICINE

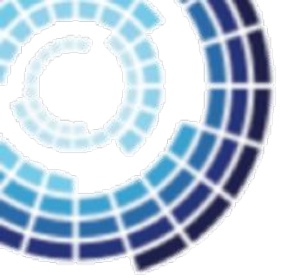
**Department of
BioMedical Informatics**

Charles Yu
PI: Dr. Jejo Koola

Using Digital Phenotyping to Assess Cognitive Status of Patients with Advanced Liver Disease

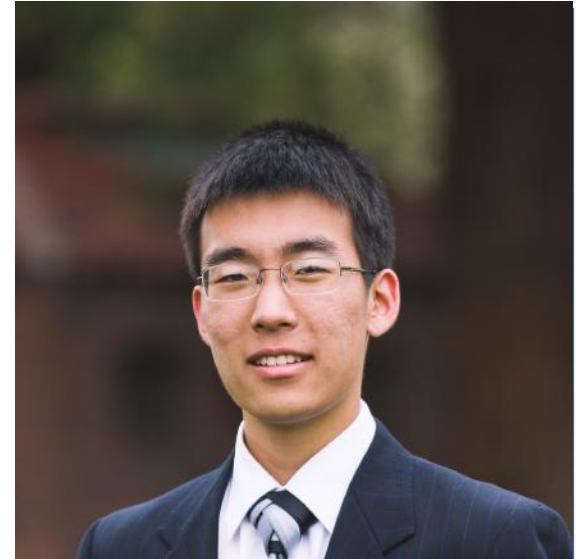
This research was supported by grant T15LM011271

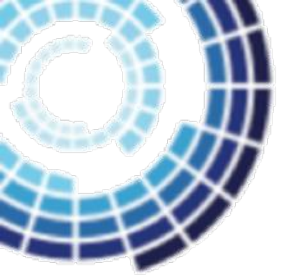




About Me

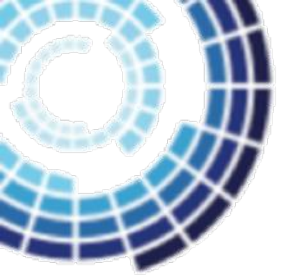
- Incoming third-year student at University of California, San Diego
- Double major in Computer Science and Probability & Statistics with a minor in Linguistics
- Academic Interests
 - Natural Language Processing – Machine reading
 - Stochastic Processes – Random walks
 - Pragmatics – Information Structure





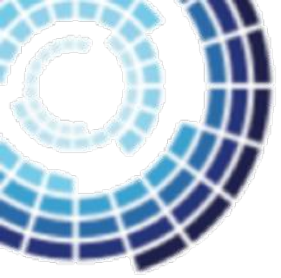
Aim of this Study

- Assess cognitive status of patients with liver disease
- Predict/Diagnose hepatic encephalopathy
- Use digital phenotyping



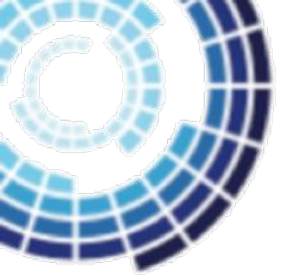
Hepatic Encephalopathy

- Hepatic – relating to the liver
- Encephalopathy – brain disease
- Hepatic Encephalopathy – neuropsychiatric abnormalities in patients with liver impairment; cognitive dysfunction due to metabolic failures caused by impaired liver function



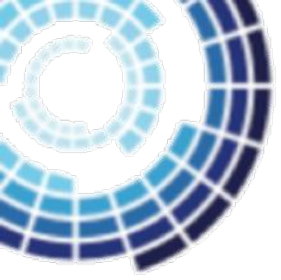
Liver Function

- Makes essential compounds for bodily function
 - Albumin
 - Blood clotting factors
 - Triglycerides
 - Glycogen
 - Bile



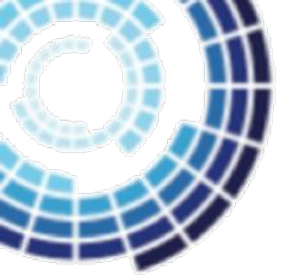
Liver Function

- Stores compounds
 - Vitamins
 - Iron
 - Cobalamin

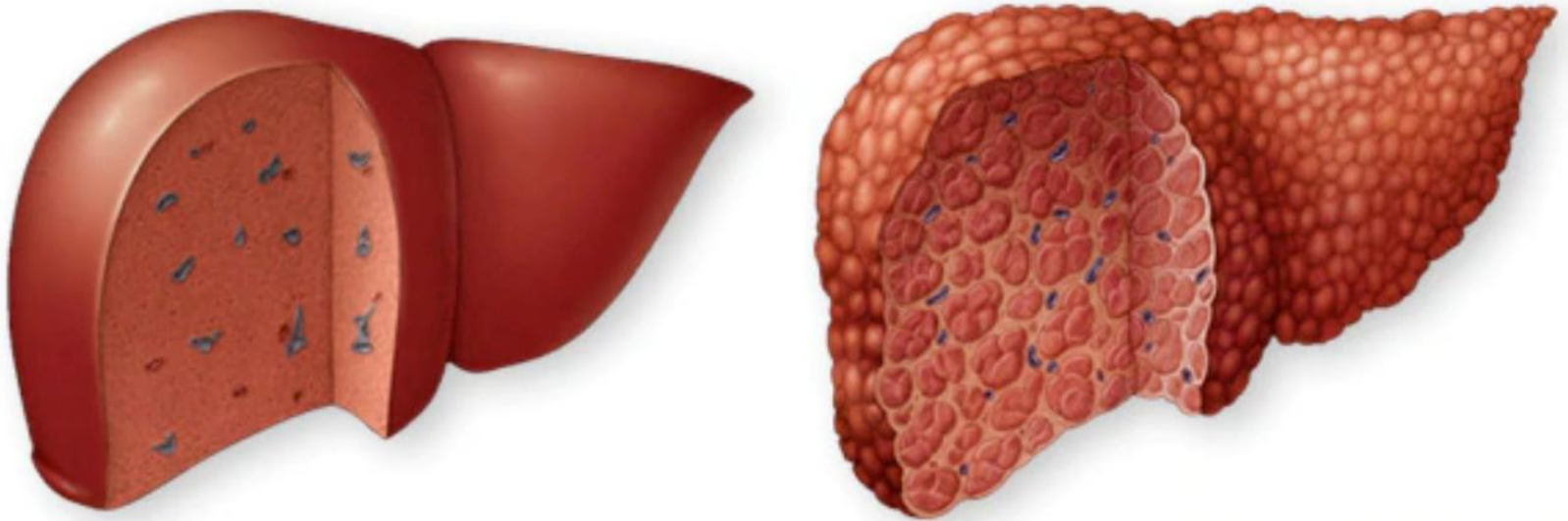


Liver Function

- Removes toxins
 - Processes medications
 - Drugs
 - Alcohol
 - Converts ammonia into urea
 - Breaks down insulin and other hormones



Cirrhosis



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Normal liver vs. liver cirrhosis

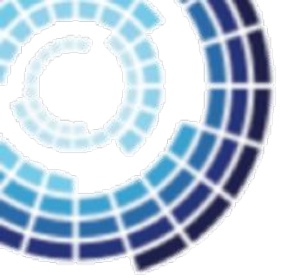
A normal liver (left) shows no signs of scarring. In cirrhosis (right), scar tissue replaces normal liver tissue.

Source: <https://www.mayoclinic.org/diseases-conditions/cirrhosis/symptoms-causes/syc-20351487>



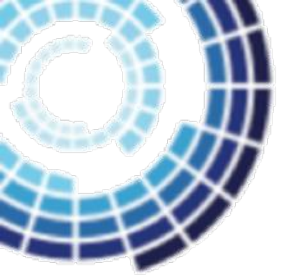
Causes of Cirrhosis

- Chronic viral hepatitis (mostly hepatitis C)
- Cystic fibrosis
- Primary sclerosing cholangitis
- Hemochromatosis
- Wilson's disease
- Diabetes
- Alcohol abuse



Cirrhosis Causes

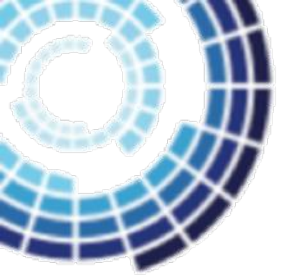
- Fatigue
- Easy bleeding and bruising
- Loss of appetite
- Nausea
- Edema in legs/feet/ankles
- Weight loss
- Itchy skin
- Jaundice
- Ascites
- Spiderlike blood vessels on the skin
- Redness in the palms of the hands
- Hepatic encephalopathy



Cirrhosis Prevalence

- 700,000 people in the United States have cirrhosis
- Nearly 70% unaware

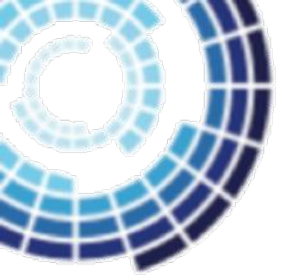
(Scaglione S, Kliethermes S, Cao G, Shoham D, Durazo R, Luke A, et al. The epidemiology of cirrhosis in the United States: a population-based study. *J Clin Gastroenterol*. 2015;49:690-696. doi: 10.1097/MCG.0000000000000208)



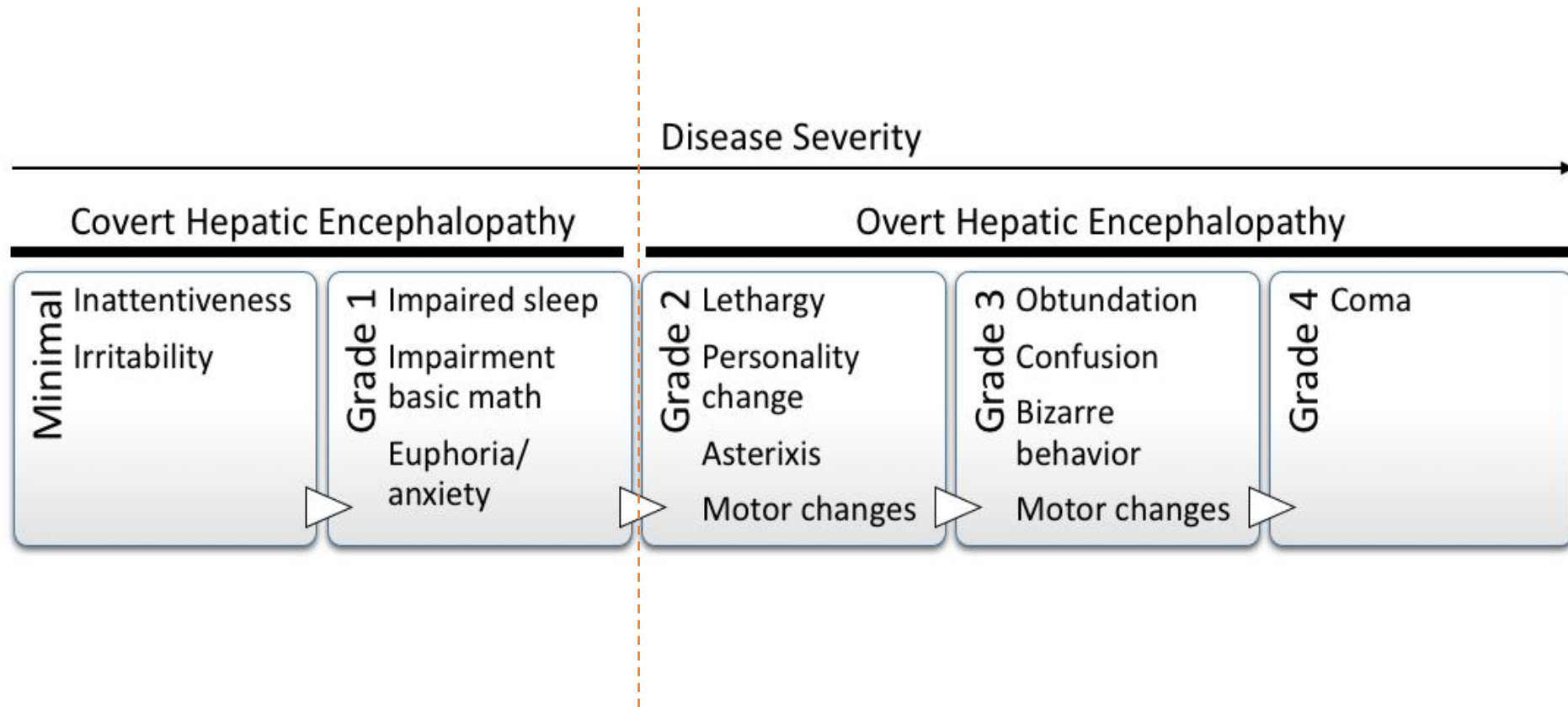
Cirrhosis -> Hepatic Encephalopathy

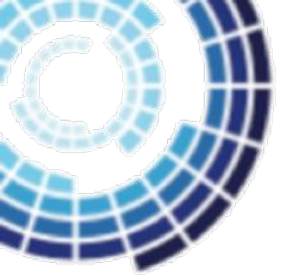
- Development/progression to hepatic encephalopathy high
- One-third have some degree of mild/subclinical hepatic encephalopathy
- One-third have clinically apparent hepatic encephalopathy

Source: Mayo Clinic



Severity of Hepatic Encephalopathy





How do we diagnose hepatic encephalopathy when the patients don't realize their symptoms might be because of it?

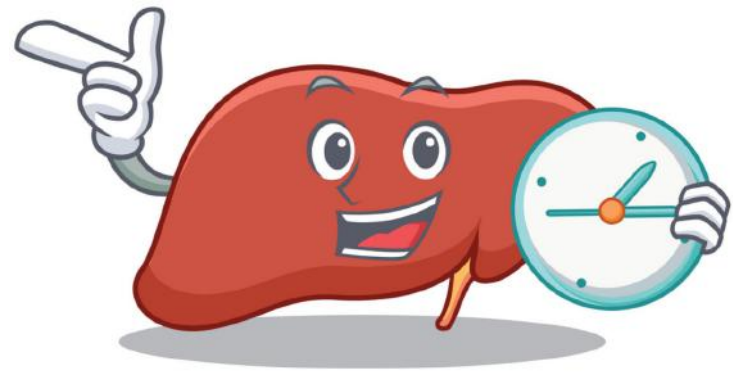


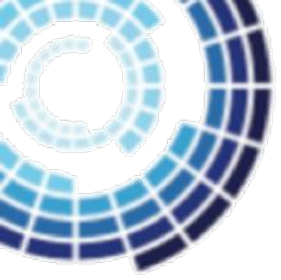
Current method of diagnosis

- Time consuming
- Require a doctor or expert to conduct many tests
- Must be done at an in-person clinic visit
- Those around the patients must bring them to the clinic



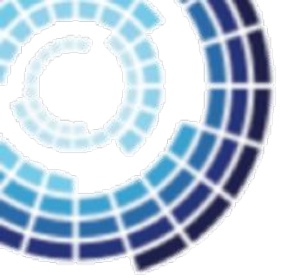
How do we treat hepatic encephalopathy before patients and those around them realize something is wrong?





How do we treat hepatic encephalopathy before patients and those around them realize something is wrong?

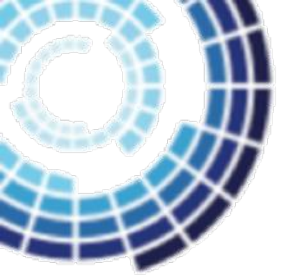
Digital Phenotyping



What is Digital Phenotyping?

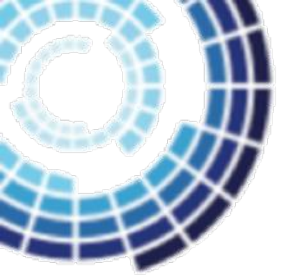
- “the moment-by-moment quantification of the individual-level human phenotype in situ using data from personal smartphones” – Jukka-Pekka Onnela

(Onnela JP, Rauch SL. Harnessing Smartphone-Based Digital Phenotyping to Enhance Behavioral and Mental Health. *Neuropsychopharmacology*. 2016 Jun;41(7):1691–6. doi: 10.1038/npp.2016.7. Epub 2016 Jan 28. PubMed PMID: 26818126; PubMed Central PMCID: PMC4869063.)



Passive Data from Digital Datastreams

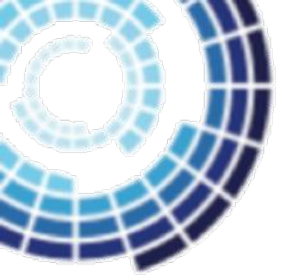
- Noninvasive
- No-to-little added effort from patients
- Smartphone data
- Wearable technology data



Smartphone Data

- Keyboard
 - Sessions
 - Keystrokes
 - Autocorrection
 - Deletion
- Accelerometer

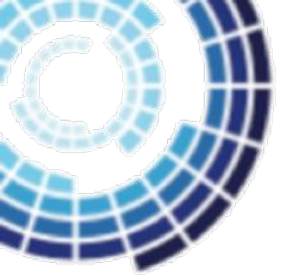




Wearable Technology

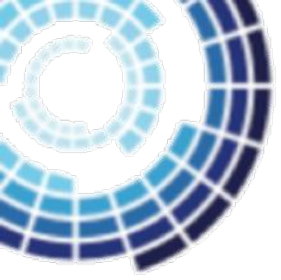
- Fitbit
 - Sleep stages
 - Sleep time
 - Charging frequency
 - Calories
 - Steps
 - Heart rate
 - Intense physical activity





Indications of HE

- Keyboard
 - Type less
 - Autocorrect more
 - Make more mistakes
 - Fewer sessions
- Accelerometer
 - Orientation (position of phone usage)
 - Movement of patient



More Indications of HE

- Fitbit
 - Sleep more
 - More erratic sleep stages
 - Charging less
 - Fewer calories
 - Fewer steps
 - Less physical activity
 - Implicit data
 - Forgetting to wear



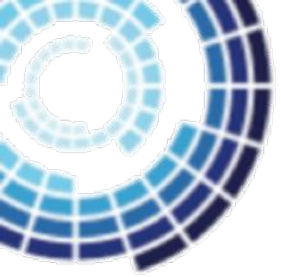
Supplements for Study

- Formal examinations
 - Clinic visits
 - Psychometric Hepatic Encephalopathy Score (PHES)
 - Stroop test
 - Inhibitory Control Test (ICT)
 - Lab tests – blood panels
 - Model for End-Stage Liver Disease (MELD) Score
 - Self-administered
 - Stroop test

GREEN

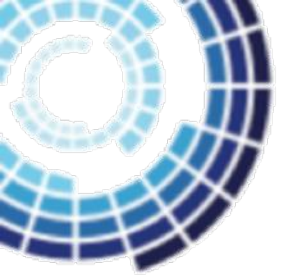
BLUE

RED



Benefits

- Save time
 - Fewer “unnecessary” clinic visits
- Save money
 - Fewer “unnecessary” clinic visits
- Patients, like us, would spend most time at home or work
 - Up to the people around them to realize something’s wrong
 - Can track patients when not at the clinic



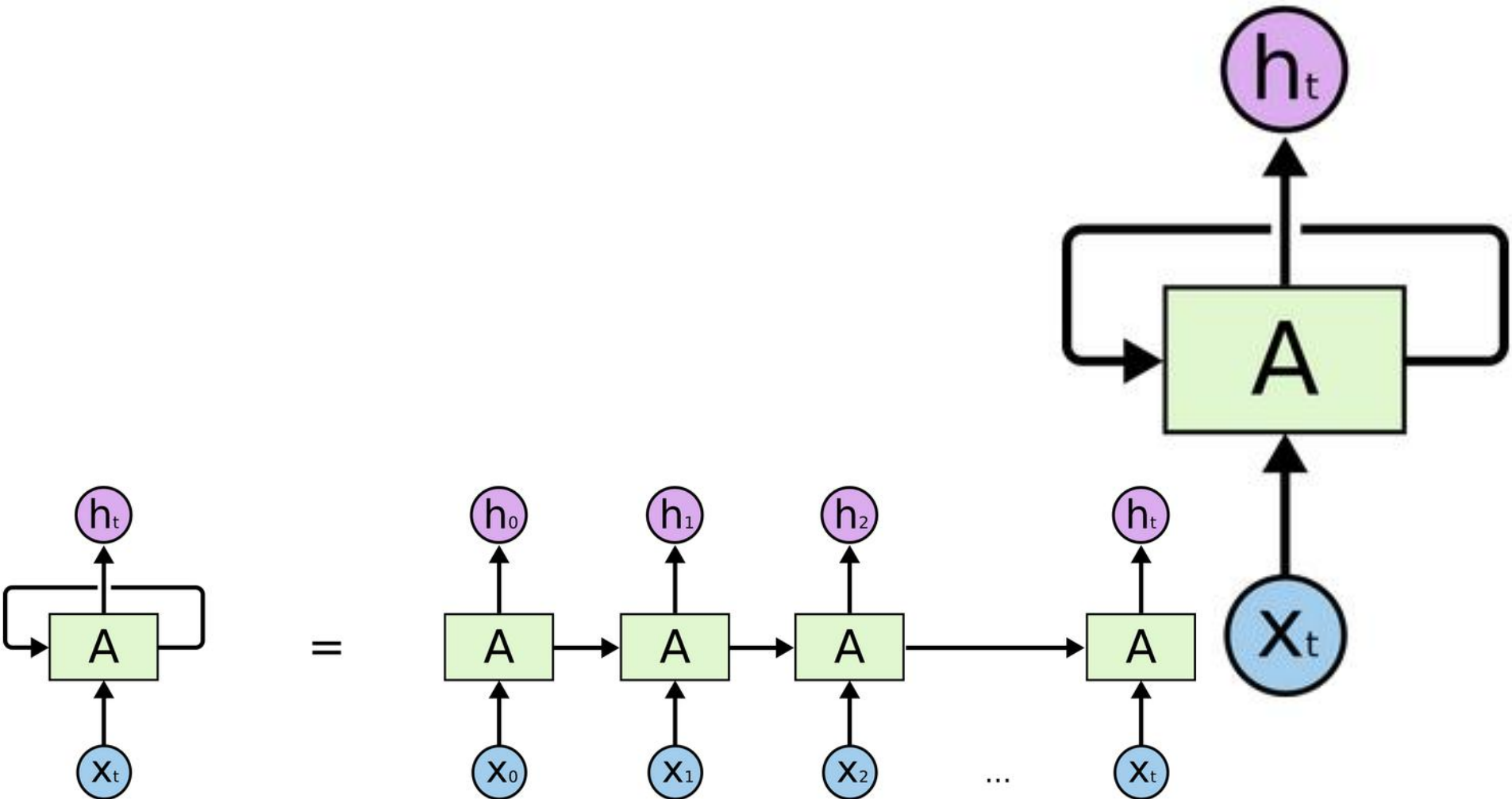
How to Interpret and Use Digital Datastreams

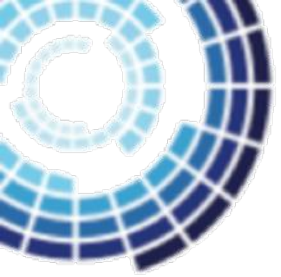
- Machine Learning and Artificial Neural Networks
 - Recurrent Neural Networks (RNN)
 - Long Short-term Memory (LSTM)
 - Gated Recurrent Units (GRU)

All proceeding figures and diagrams source: Olah, Christopher.
<https://colah.github.io/posts/2015-08-Understanding-LSTMs/>

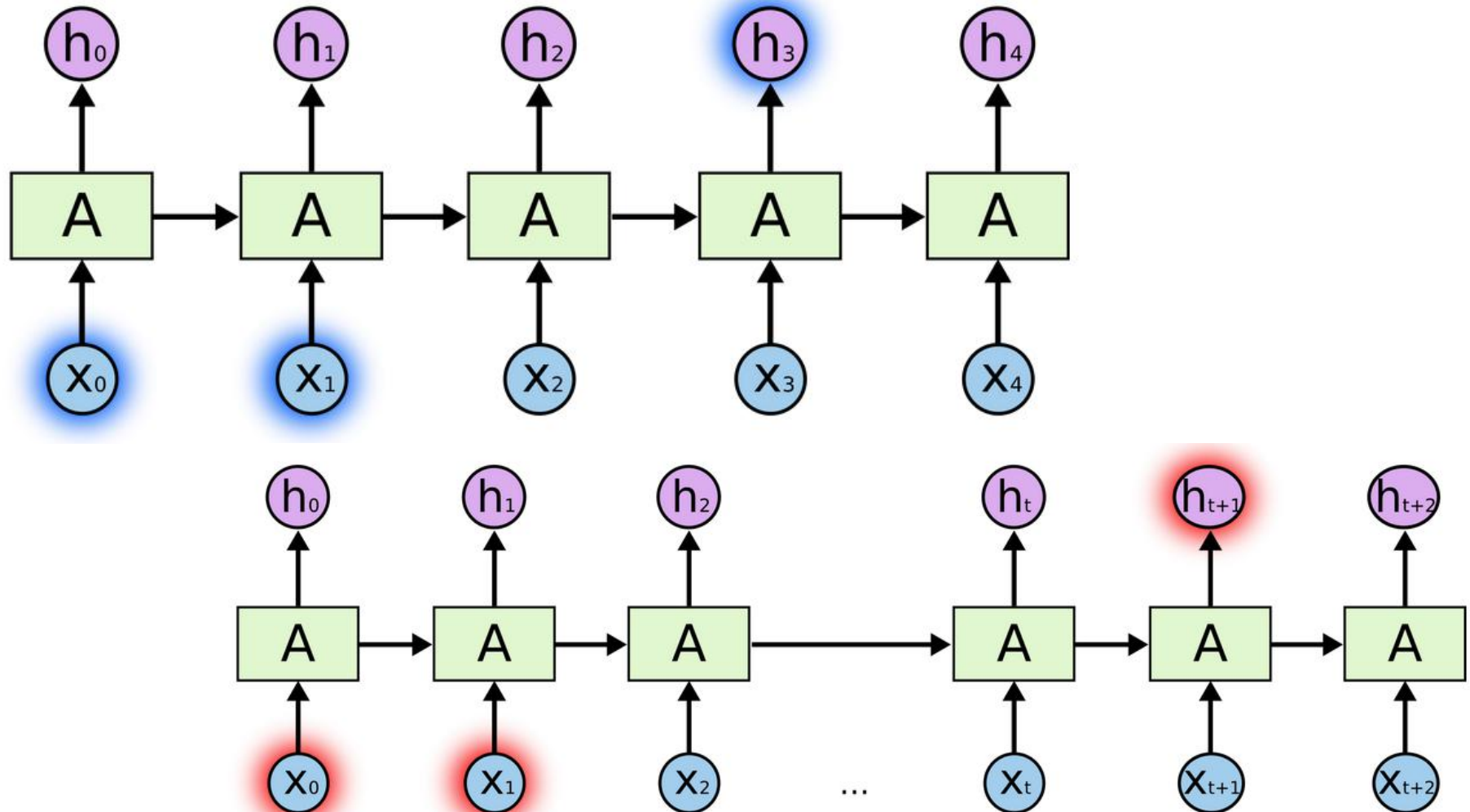


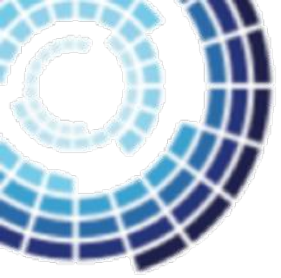
Recurrent Neural Networks



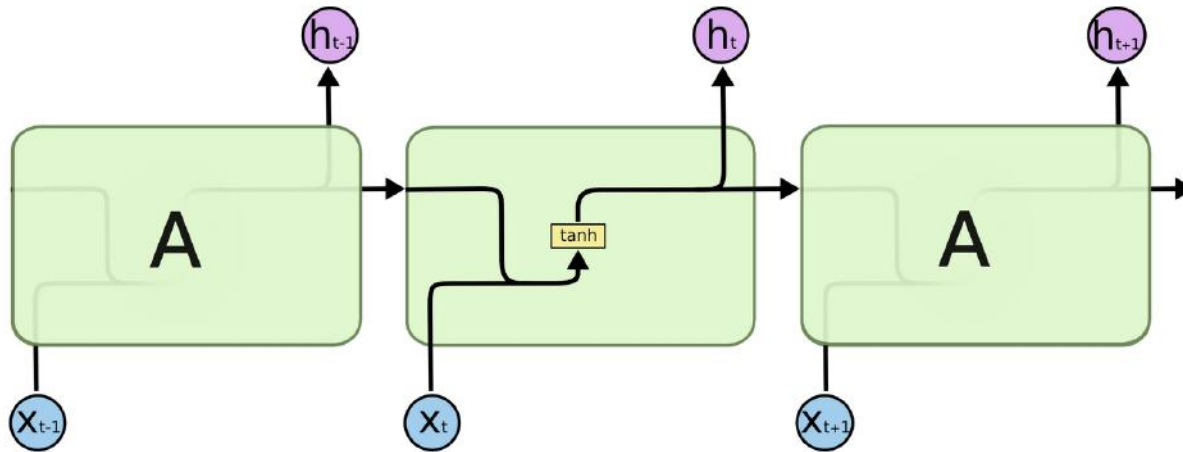


Recurrent Neural Networks

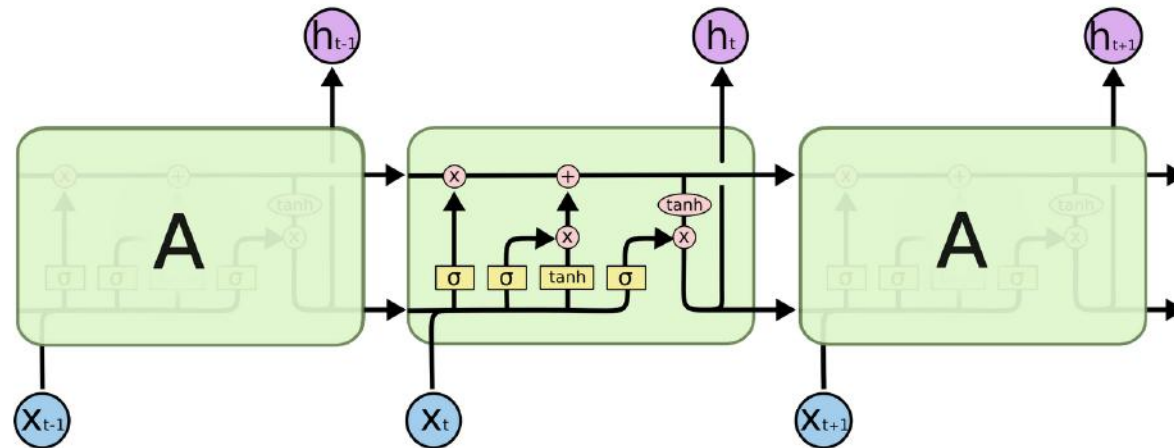




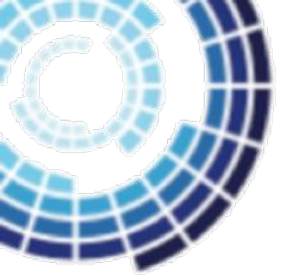
Long Short Term Memory Networks



The repeating module in a standard RNN contains a single layer.

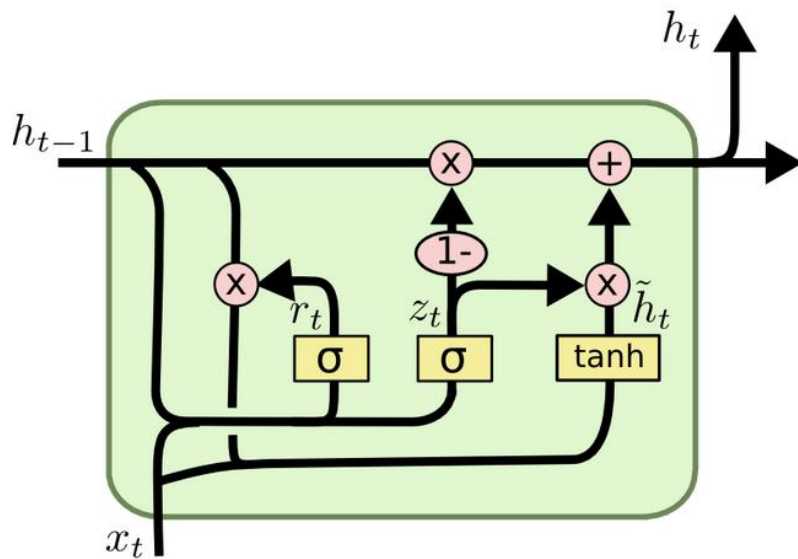


The repeating module in an LSTM contains four interacting layers.



Gated Recurrent Unit

- Cho, et al. Learning Phrase Representations using RNN Encoder–Decoder for Statistical Machine Translation



$$z_t = \sigma (W_z \cdot [h_{t-1}, x_t])$$

$$r_t = \sigma (W_r \cdot [h_{t-1}, x_t])$$

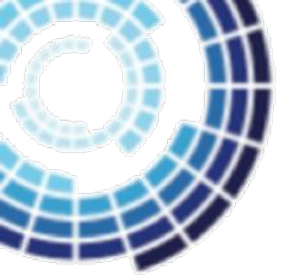
$$\tilde{h}_t = \tanh (W \cdot [r_t * h_{t-1}, x_t])$$

$$h_t = (1 - z_t) * h_{t-1} + z_t * \tilde{h}_t$$



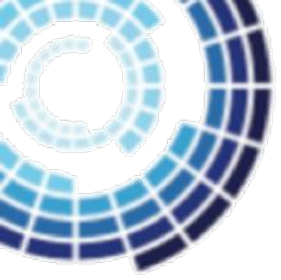
Benefit of Using These

- Long-term dependencies
 - Changes relating to each patient, not relating to some general average
 - Longitudinal/time series



Next Steps

- Get more patient data
- Keep training our models
- Adjust hyperparameters
- Scale this study
- Generalize this study design



What I learned

- Legal and ethical use of protected health information
- How to structure and conduct a research study
- How to structure and write a research paper
- Gained experience with collecting data with electronic data capture software
- Gained experience with data wrangling



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Acknowledgements

- Dr. Jejo Koola
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Questions?