AI & Machine-learning in Physicians' Workflows

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Introduction

"The CMIO role is gradually being transformed, particularly in more advanced health organizations, from its early 'tech-head doc' role,
to a management role in IR implementation,
to a transformational leadership role,
to a role catalyzing discovery and translational research. Skills are needed to help lead <u>discovery</u>."

Introduction

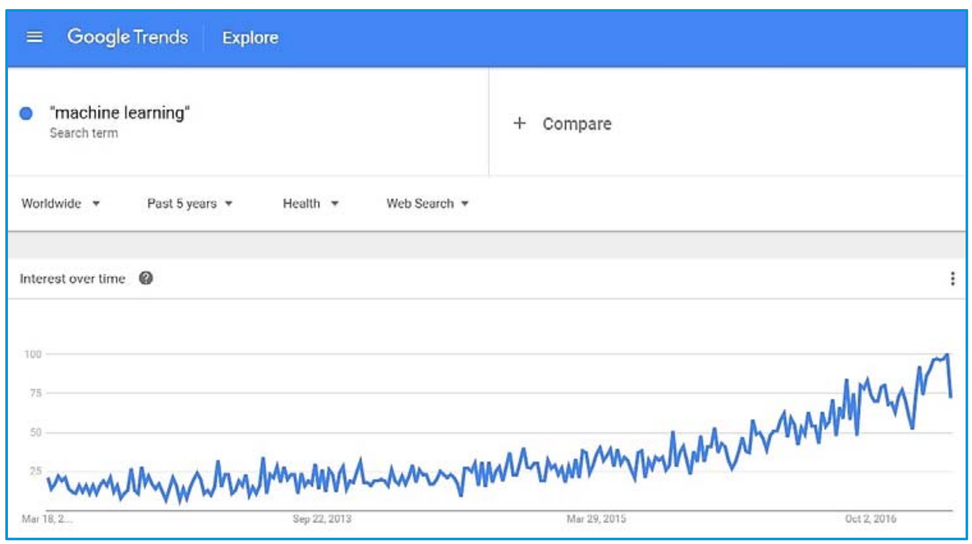
- Evolution of CMIO role:
  - Beyond electronification of paper was quality and value (triple aim)
  - Beyond quality and value was enhancement of clinician experience
  - Beyond clinician experience is discovery via machine-learning and AI
- Confidentiality-protected, de-identified health records and registries enable new capabilities for observational research and discovery
- Most, if not all, of the opportunities to create value with data involve mathematical equations, classification or prediction models, or statistical patterns
- Most involve ‘machine-learning’ from observational data
- These are not your granddad’s “IF-THEN” CDS algorithms

Definitions

- Artificial Intelligence (AI)
  - Computational emulation of effective goal-oriented behavior, often with deliberation and intention
- Machine Learning (ML)
  - Several dozen methods of empirical pattern detection

Factors that motivate ML – why, when, how

- Data missingness, rapid change, high-dimensionality, ‘ensemble’ robustness
- Curse of dimensionality — evaluating every feature can reduce not only the speed of classifier training and execution, but reduces predictive power
- Unlike neural networks and some other ML methods, others like AdaBoost, Random Forest, and LASSO retain only those features that improve the predictive power of the model
- Biases, unbalanced data (things that cause conventional statistical models to go astray)



ML to predict AKI before it materializes

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Previous approaches' limitations

- Blood tests
  - Predictions confounded by variations in body composition, metabolism
  - Wide within-patient variability based on evolving patient management, fluids, etc.
  - Lagging indicators of renal deterioration
  - Creatinine changes significantly only when ~ 50%+ of function is lost
- Urine tests
  - Time-averaging by mixing/dilution in bladder ➔ poor sensitivity
  - Lagging indicators of renal deterioration

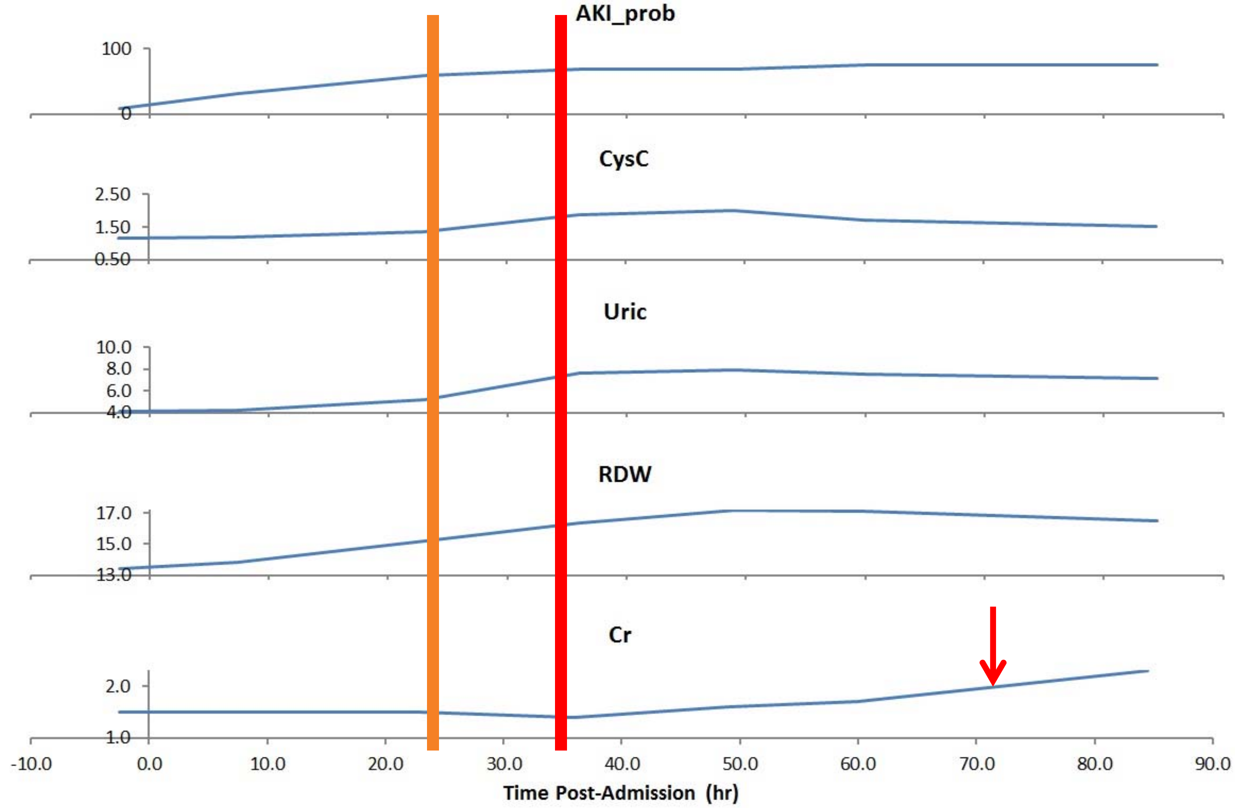
AKI ML

- 40,000 inpatient AKI cases and 40,000 non-AKI inpatient controls
- Random Forest discovery of 3 parameters that are leading indicators
- Time series model combines velocity and doubling-time metrics
  - Serum creatinine or cystatin C
  - Serum uric acid
  - Red blood cell distribution width (RDW%)

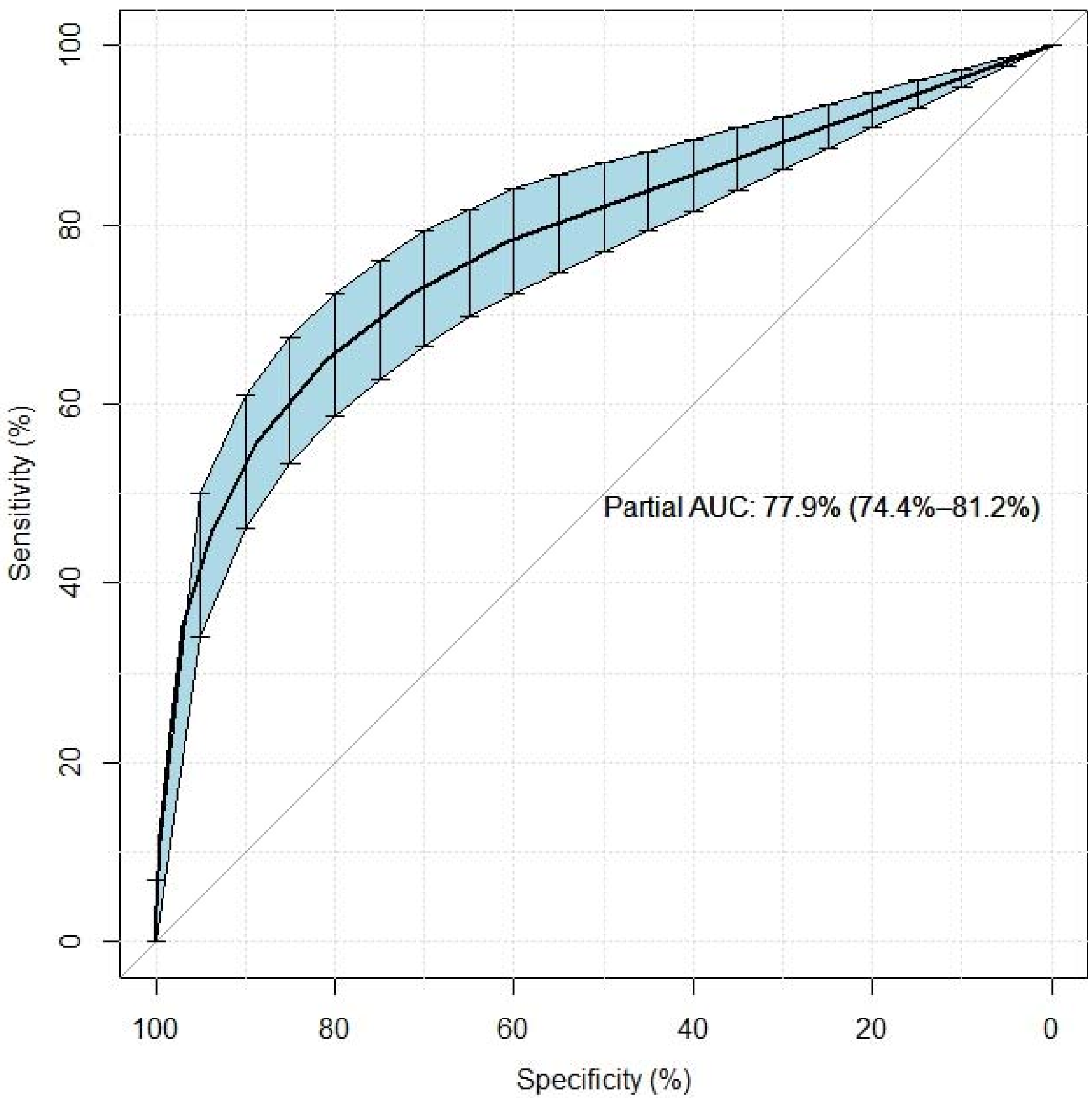
  (Other temporal metrics have poor sensitivity/specificity or require longer time series)
- Addresses assessment of risk of acute deterioration
  - Math predictive model only requires at a minimum 3 time points
  - Preferably 4 or more time points
  - Doubling-time ascertainment requires at least 4 time points
- Integrates with flowsheet clinician workflow
- Can trigger CDS initiation of prevention or AKI management ordersets

Example AKI pattern

post_adm (hr)	CysC (mg/L)	uric (mg/dL)	RDW (%)	Cr (mg/dL)	AKI prob (%)
-2.5	1.16	4.1	13.4	1.5	8
7.4	1.19	4.2	13.8	1.5	31
23.0	1.34	5.2	15.2	1.5	$\boxed{59}$
36.0	1.89	7.6	16.4	1.4	$\boxed{68}$
49.0	2.01	7.9	17.2	1.6	68
60.0	1.70	7.5	17.1	1.7	76
84.5	1.53	7.1	16.5	2.3	76



ROC - AKI prediction



Forecast ED Crowding with ML

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Motivation

- ED congestion adverse health outcomes
- Patient experience with long and unpredictable waiting times
- ED service managers lack means for accurately predicting or preventing or managing the severity or duration of congestion
- Aim:
  - Determine quantitative ‘self-similarity’ properties of inter-arrival interval time series
  - Discover fractal ‘self-similarity’ pattern to forecast congestion
  - Provide managers with choices that will prevent or abate congestion

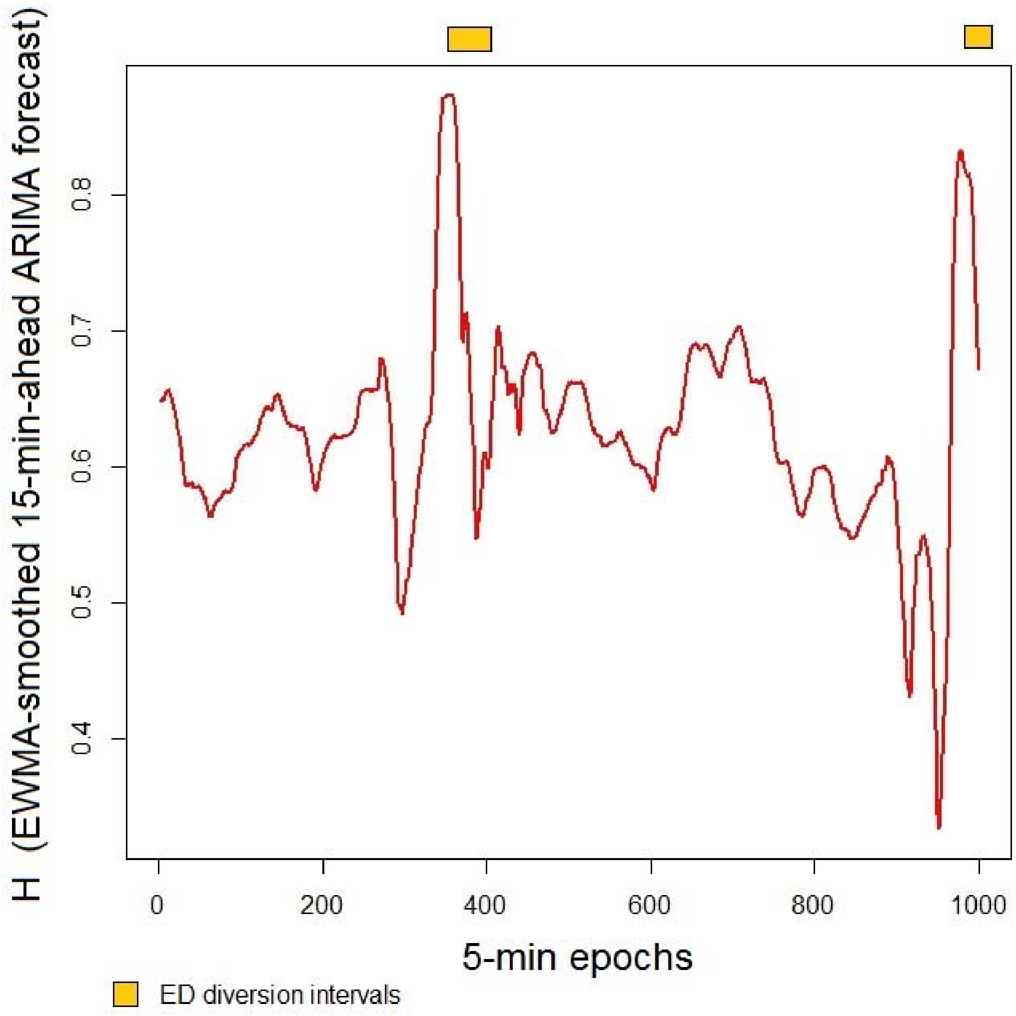
Prior approaches' limitations

- Fail to determine the patient-arrival, -care, and –departure processes
- Fail to determine the resource sourcing processes
- Require information that is either not available or updated frequently
- Lagging indicators that do not help prevent
- Fail to take into account finite bed capacity (saturation)
- Fail to account for dependencies between labor supply and demand

Forecasting congestion before it arrives

- Retrieve recent historical arrivals event time series data (e.g., previous 120 minutes' arrivals) for the service process of interest.
- Count arrival events accruing in consecutive time periods or epochs (e.g., epochs of 5-min length).
- Forecast congestion via fractal Hurst exponent time-series
- If the forecast Hurst exponent exceeds 75^{th} percentile of ED length of stay, then emit message to ED manager

Example



H (EWMA-smoothed 15-min-ahead ARIMA forecast)
0.4
0.5
0.6
0.7
0.8
0
200
400
600
800
1000
5-min epochs
ED diversion intervals

ED congestion forecasting

- ML model dynamically re-characterizes supply and demand processes for each resource
- Does not require constant updating by staff in other parts of the hospital
- Far simpler than NEDOCS and other approaches
- Reliably predicts future congestion 30 to 120 min ahead
  - Associated with ED Length of Stay (LOS) exceeding 75th percentile

ML for Tremor Management in Parkinson's Disease

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Tremor management pharmaceutics in PD

- Carbidopa, L-dopa (1:4)
- Entacapone/tolcapone (COMT inhibs)
- Amantadine/rimantidine
- Rasagiline/selegiline (MAO-B inhibs)
- Benztropine/trihexyphenidyl (anticholinergics)
- Pramipexole/ropinirole/rotigotine/apomorphine (dopamine agonists)
- Pergolide/bromocryptine (ergot)
- Primidone/topiramate (anticonvulsants)
- Cannabidiol/dronabinol
- Botox injections

Management of motor fluctuations in PD

- Adjust levodopa
  - Change incremental dose and interval
  - Different formulation
- Add adjunctive agent(s)
  - Amantadine, MAO-B inhibitor, COMT inhibitor, Dopamine agonist, Anticholinergic, Anticonvulsant
- Injectable apomorphine as a “rescue” drug

Prior approaches' limitations

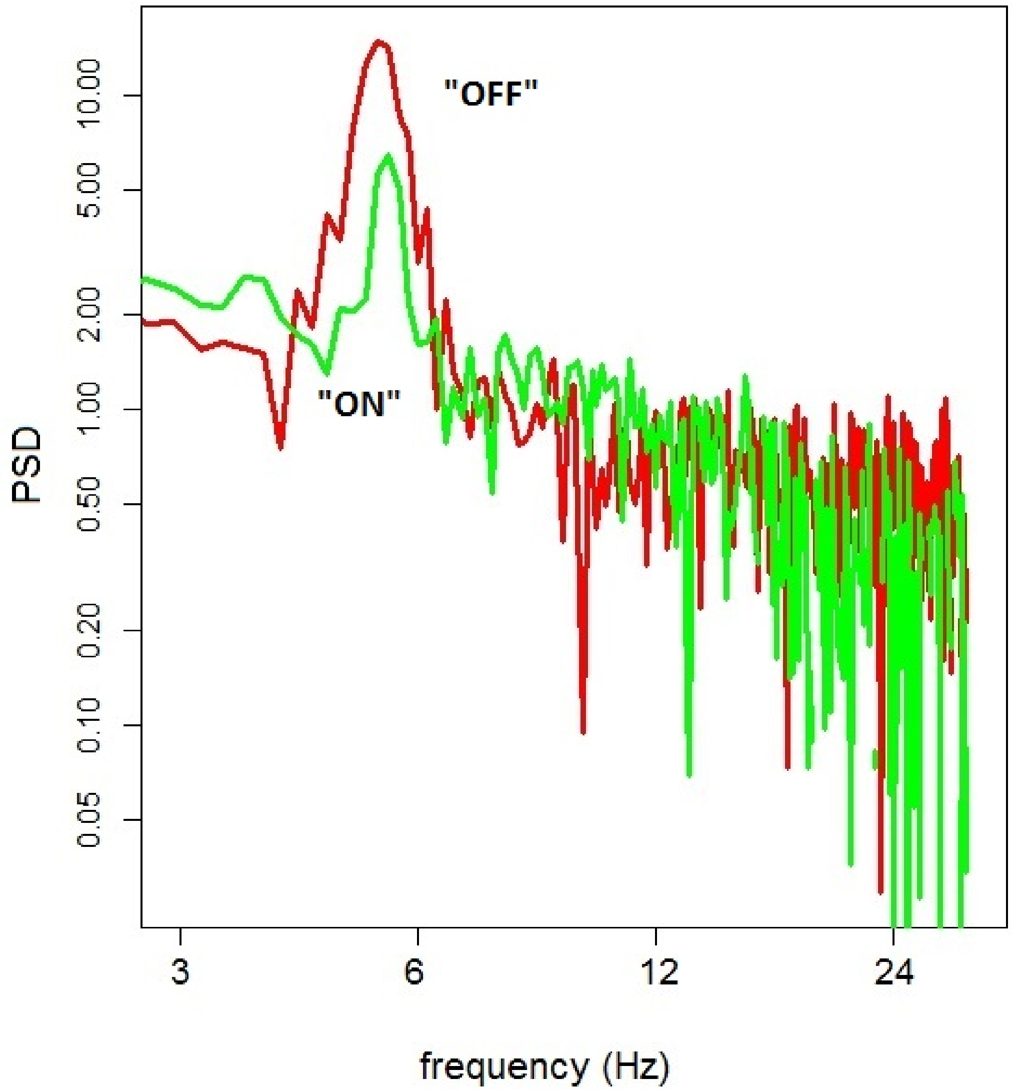
- Raw accelerometer data too insensitive, under-detect intentional/dynamic tremor
- Spiral drawing 'absolute amplitude' measurements require patient effort
- Goniometry sensors too cumbersome and require very careful placement
- Time-consuming, long measurement intervals
- Equipment was expensive and "fussy" to use
- Inadequate characterization of circadian variations in tremor intensity
- Unable to distinguish essential tremor from Parkinson's and 'mixed'
- Frequency bands of tremors
  - Resting (1-7 Hz)
  - Postural (8-15 Hz)
  - Kinetic (various freq bands; 20+ Hz)

ML of accelerometry waveforms

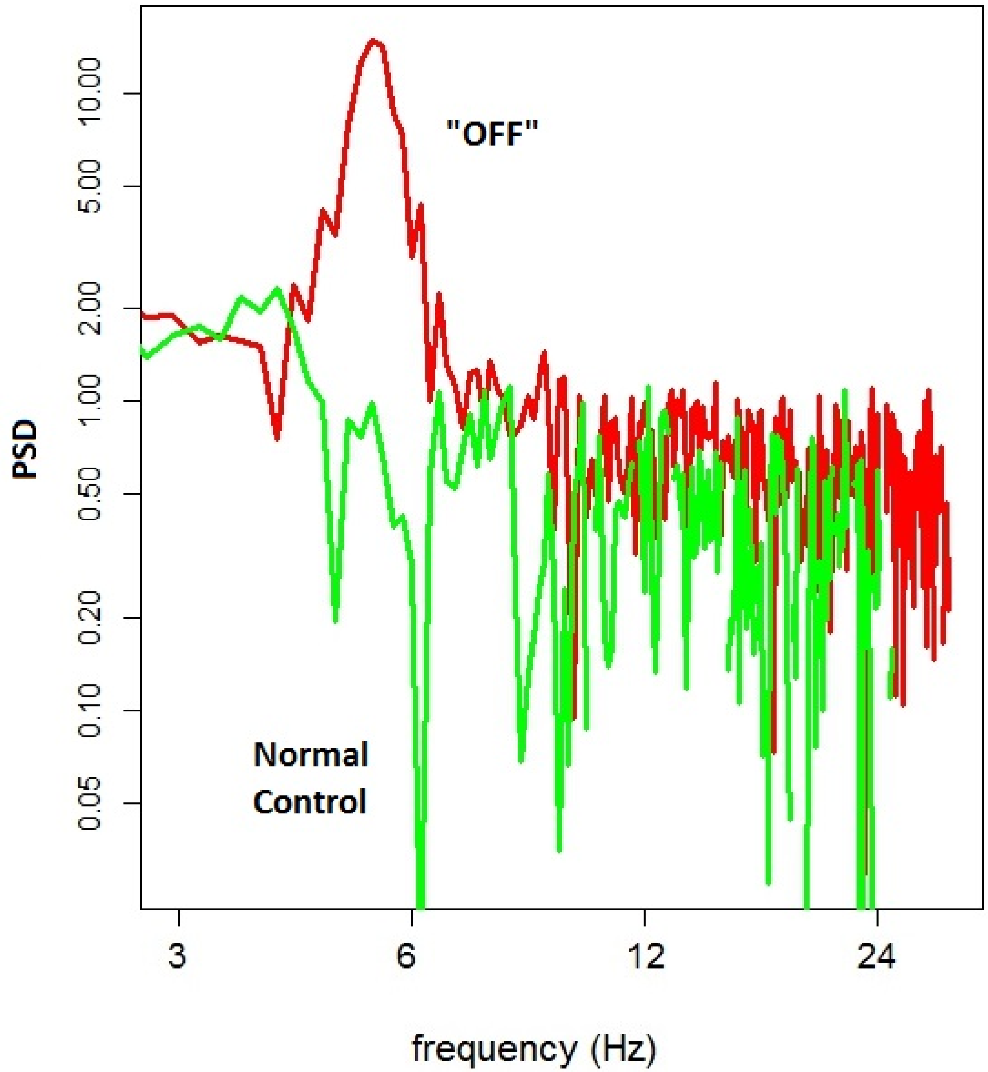
- Inexpensive wearable sensor device
- Initial clinical trial: neurology clinic use
  - Subsequent clinical trial: home use qid
- Telemetry of multiple 60-sec 3-axis accelerometer time series
  - Data upload can be at any convenient time
- Power spectrum reveals details of tremor activity
  - Circadian variations in tremor
- Time-averaged power in tremor-relevant frequency band can be used to optimize treatment modalities, dosing

Sensor device in elastic band

Example – “On” meds (green) vs. “Off” meds (red)



Example – Healthy control (green) vs. “Off” meds (red)



ML for predicting hyper- and hypo-glycemic events

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Motivation

- Complications of diabetes are strongly associated with frequency and severity of blood sugar fluctuations
  - Hypoglycemia (< 70 mg/dL)
  - Hyperglycemia (esp., > 250 mg/dL)
- Aim:
  - Machine-learning identifies patterns preceding hypo-/hyper-glycemia
  - Ad hoc self-monitoring glucose measurements using existing inexpensive glucometers and strips

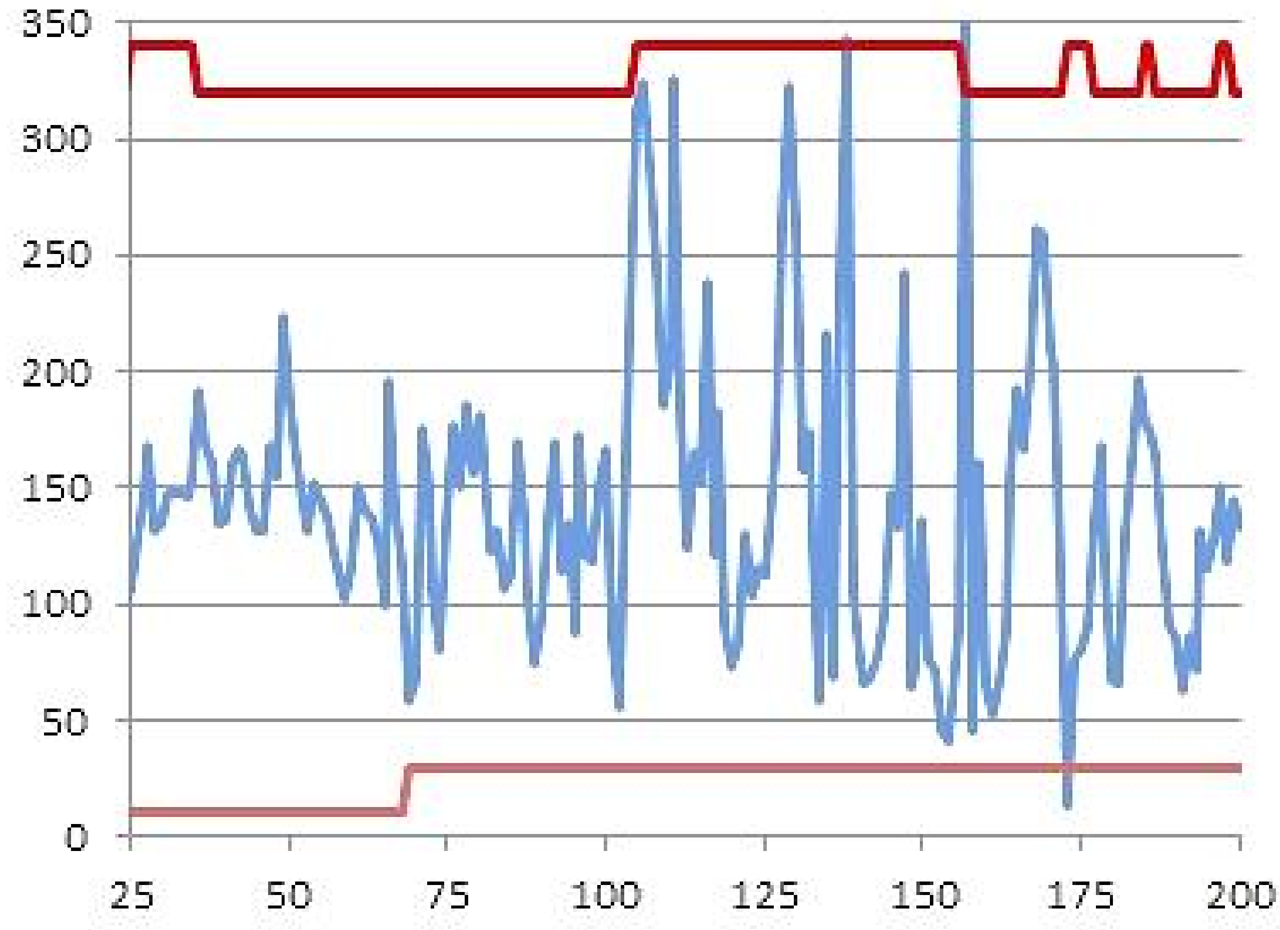
Prior approaches' limitations

- Requires high-frequency measurements (continuous, seconds timescale, indwelling percutaneous sensor) at regular, periodic intervals
- Requires detailed, ongoing recording of food intake, physical activity, insulin and other medication doses
  - Plus calculating other variables derived from these (e.g, carbohydrate to insulin ratio)
- Requires additional monitoring (cumbersome; expensive; leads to disuse)
  - Heart rate variability; Skin galvanometry; Temperature measurements; Sleep actigraphy; Step-counting accelerometry
- Requires periodic laboratory testing
  - Insulin level, C-peptide, etc.
- Accuracy is often inadequate to guide decision-making and action
  - Especially during periods of infection, etc.
- Time-horizon of forecasts is too short
- Not equally suited to diabetes cases of different severity

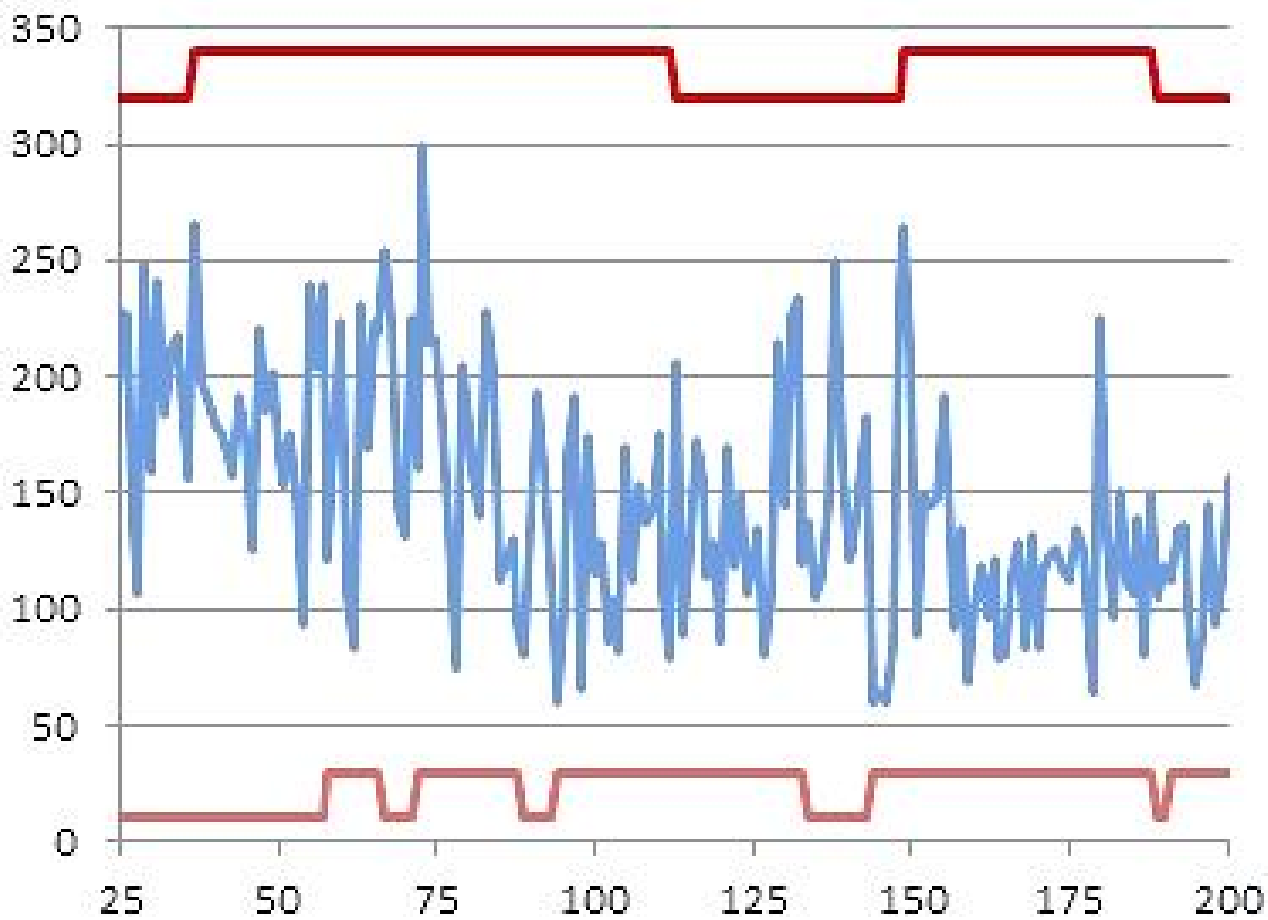
Forecasting hypo- and hyperglycemia

- Calculate the root mean square of successive deviations (RMSSD) and entropy of glucose series
- Determine signal to be emitted and specific therapy adjustment advice
  - 'Exercise is not advised for the next 6 hours';
  - 'Bring extra juice or food with you today, on account of increased risk of hypoglycemia';
  - 'Bring extra insulin with you today, on account of increased risk of hyperglycemia';
  - 'Eat a larger snack at bedtime, on account of increased risk of pre-dawn hypoglycemia'; etc.

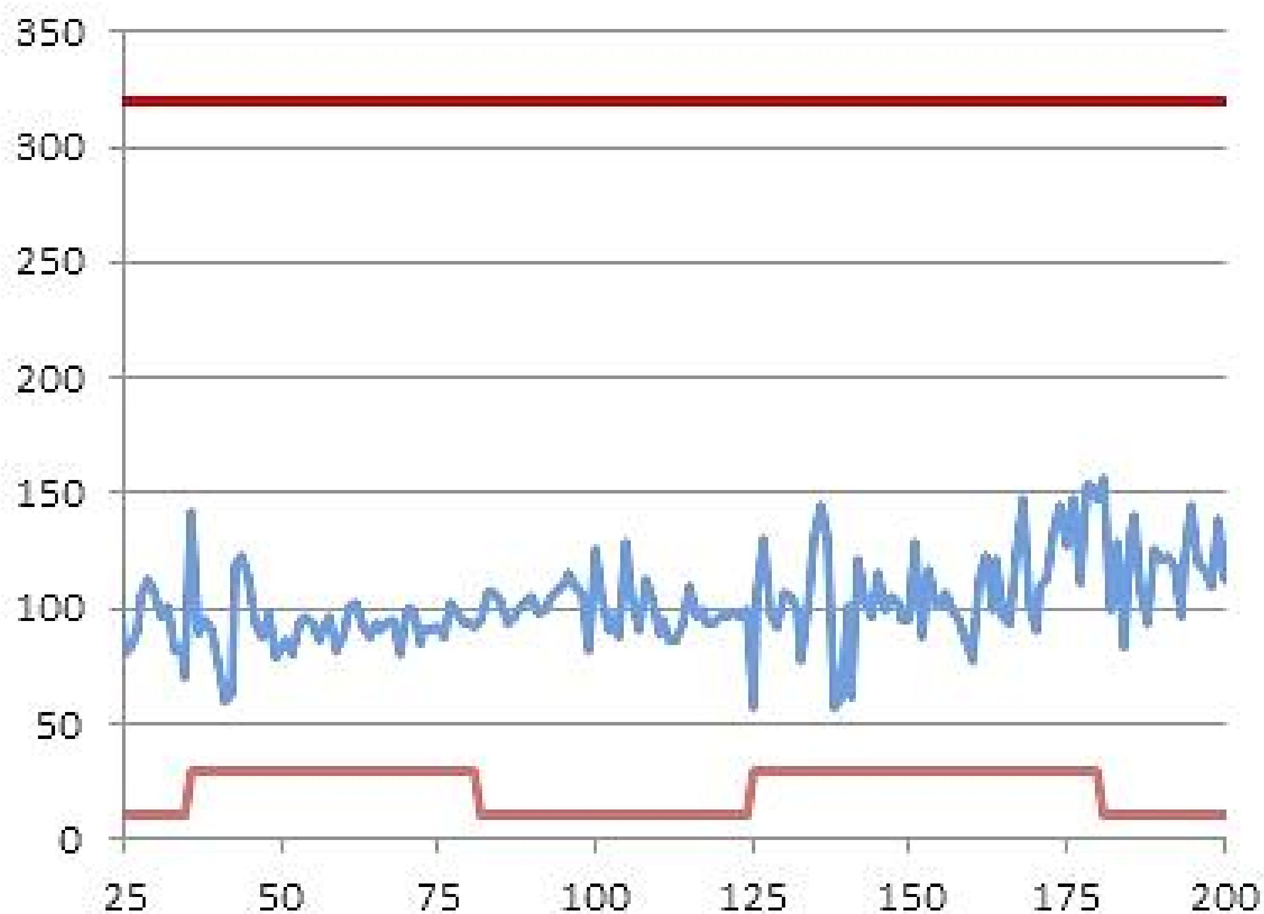
Example 17



Example 163



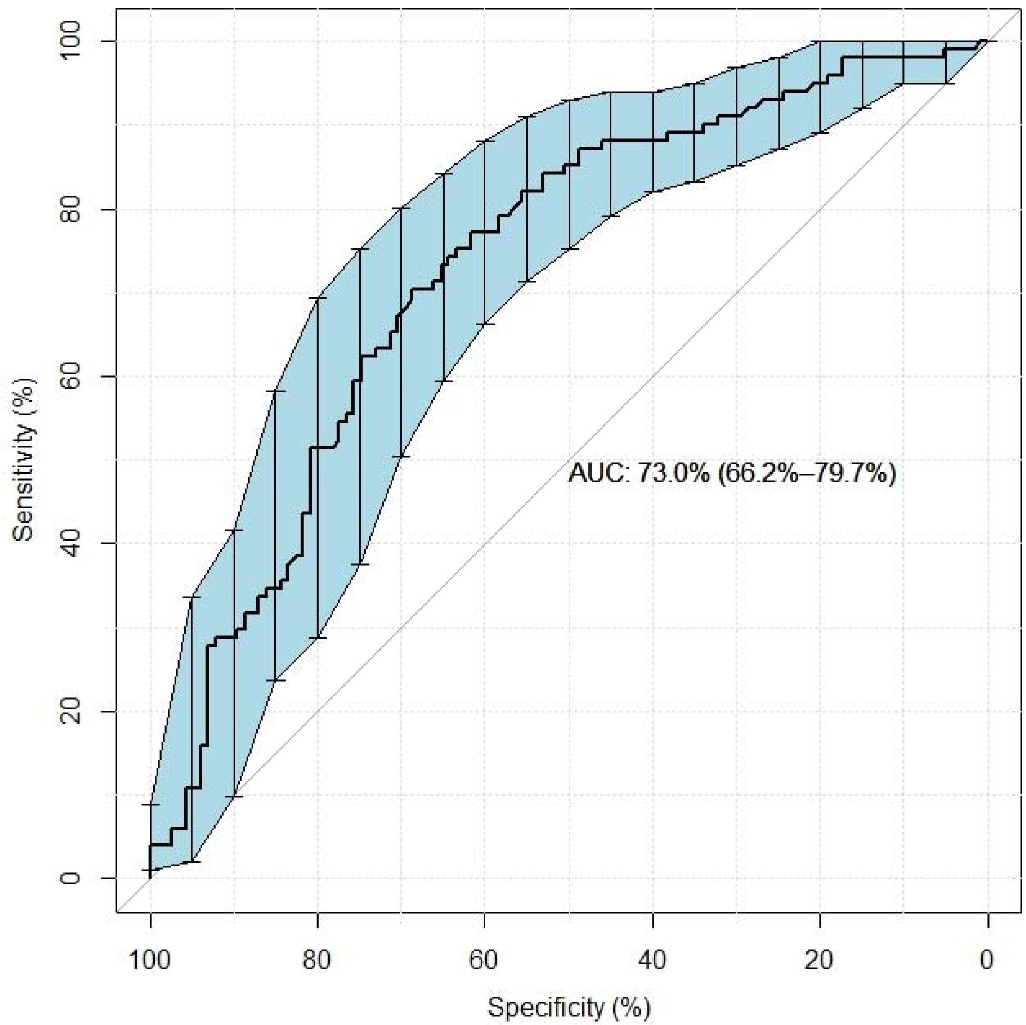
Example 169



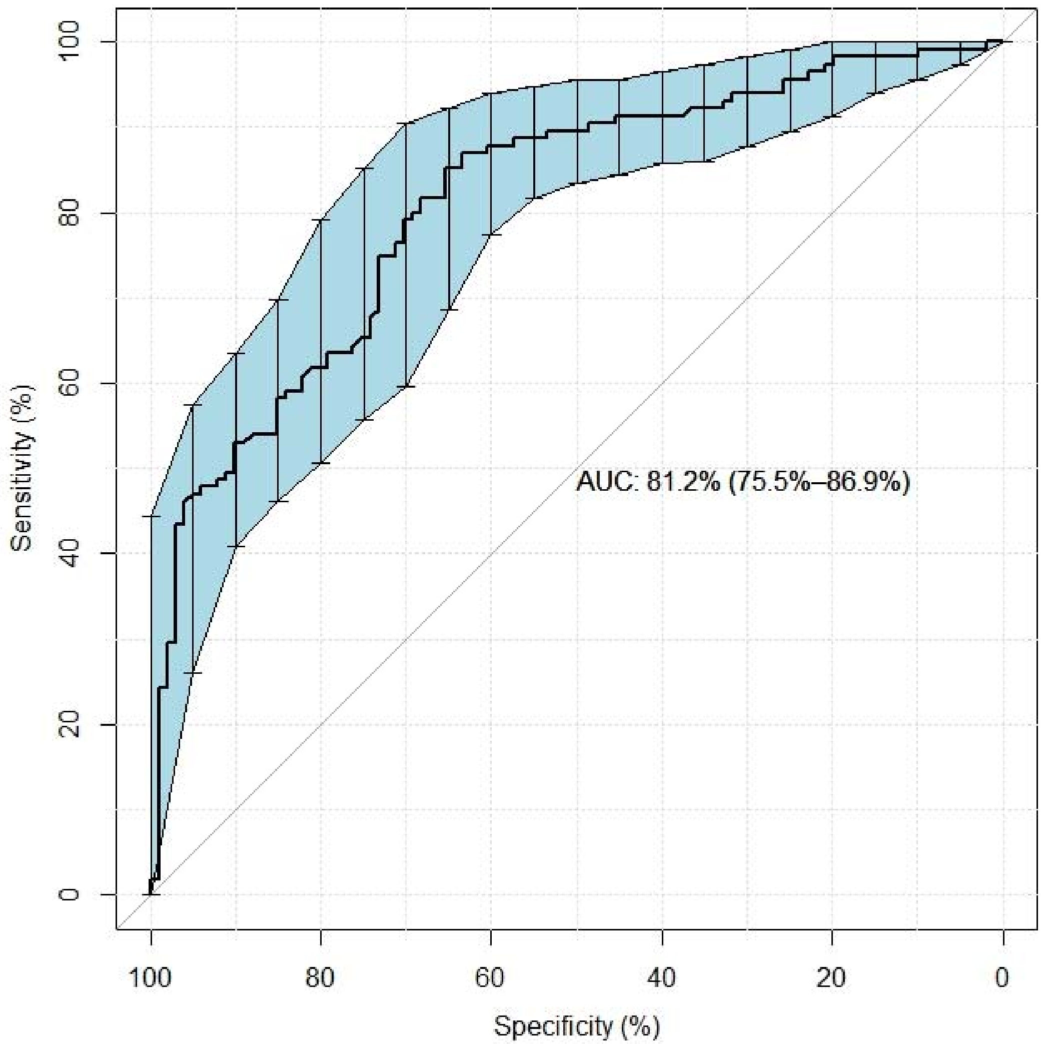
Data used for ML in diabetes

- Type 1 diabetics
  - 566,905 distinct persons (JAN-2000 through DEC-2014)
  - Many with >1,000 serial glucose measurements, all date-time stamped with minute-wise time resolution
  - Dataset does not currently distinguish ‘fingerstick’ from ‘alternate site’ (thigh, forearm, etc.) measurements
- Future modeling of Type 2 diabetics’ glucometer measurements

ROC – Hypoglycemia model



ROC – Hyperglycemia model



Comment

- ML involves quantitative measures of chaos (entropy) and spectrum analytic properties (RMSSD) of time series
- Forecasts future exceedances of low- and high-thresholds of target glucose range, enabling effective preventive maneuvers
- Predictive accuracy is sustained despite wide variations in patient's self-monitoring and adherence (or not) to prescribed therapy

ML and IoT sensor data

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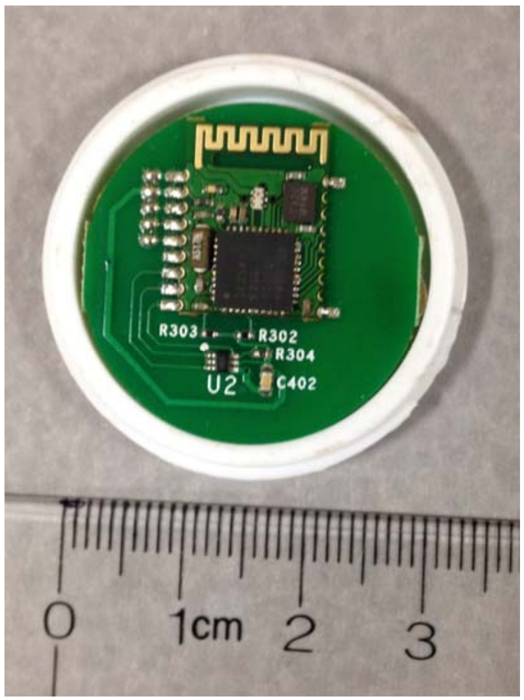
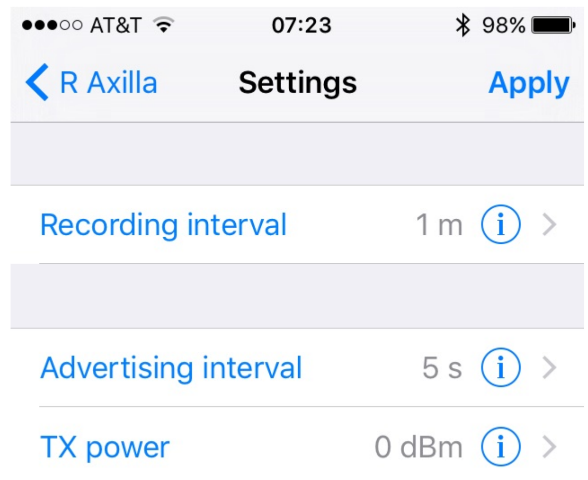
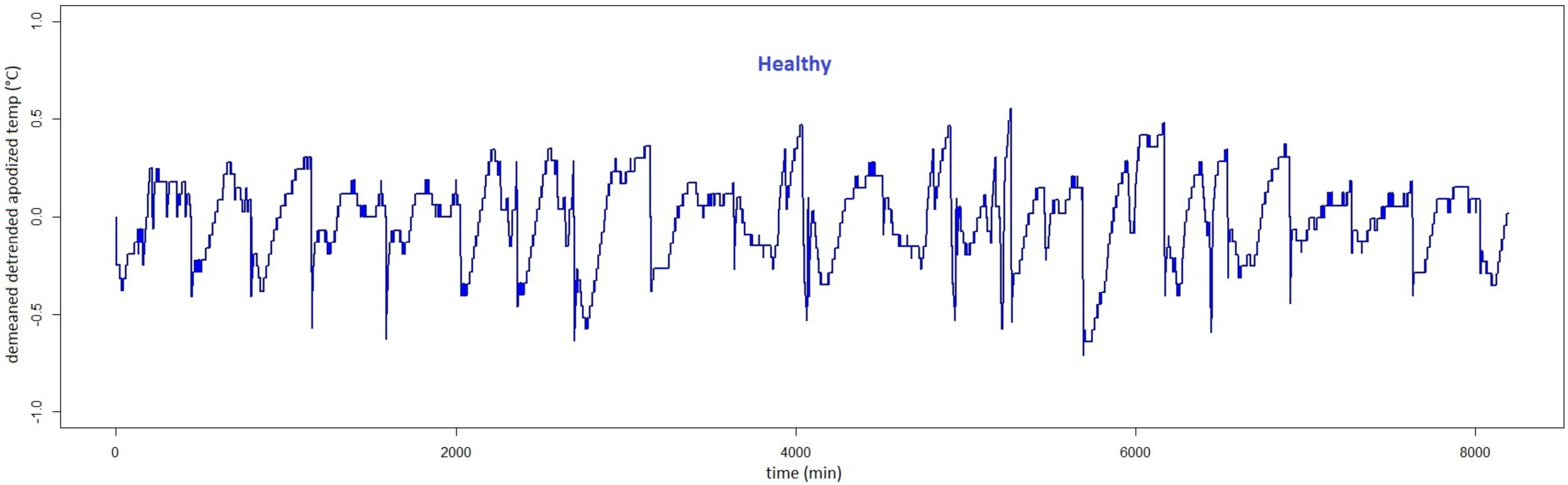
qhs BLE IoT Beacon with temp sensor in RA patients

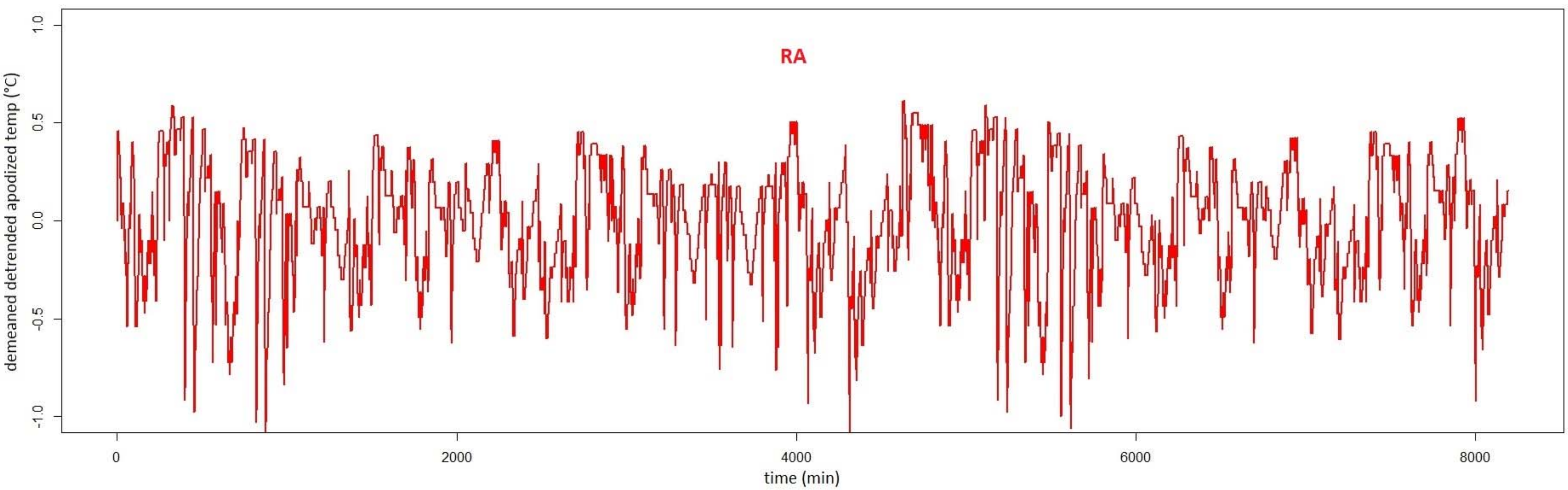




BLE IoT temp sensor beacon in RA patient before bedtime

21d healthy control vs. RA temp qhs q1m time series





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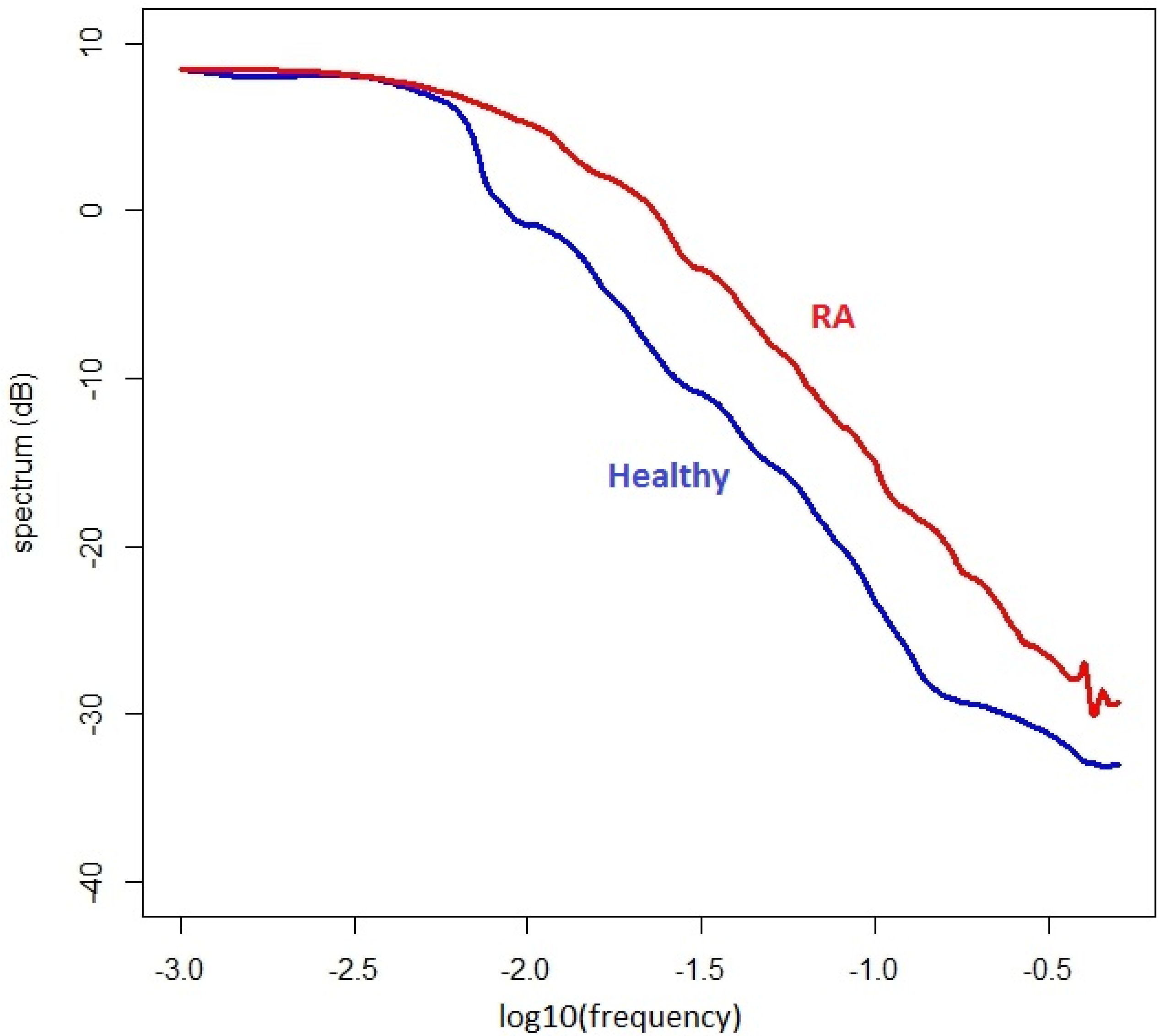
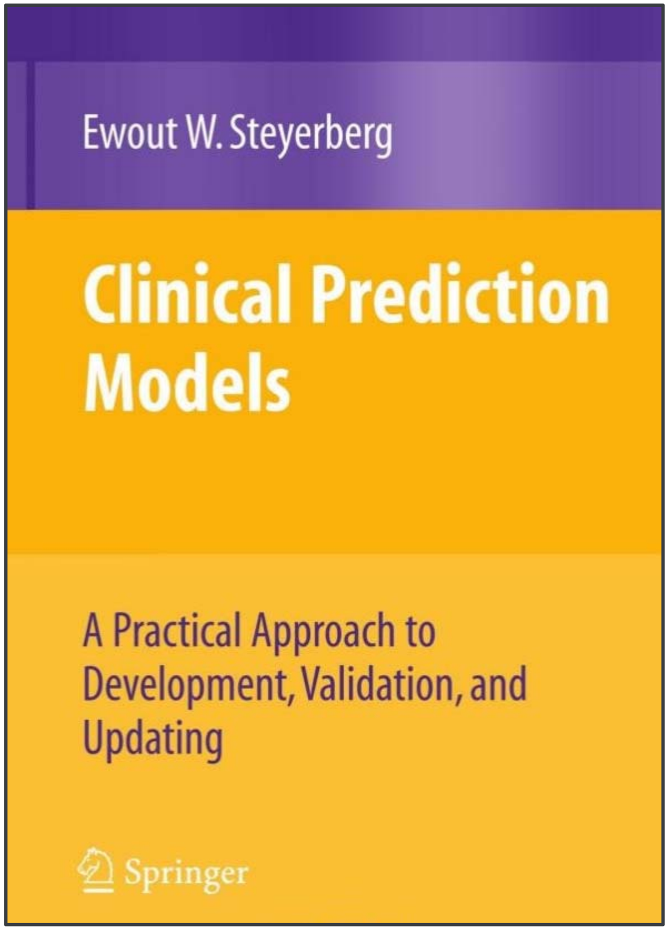
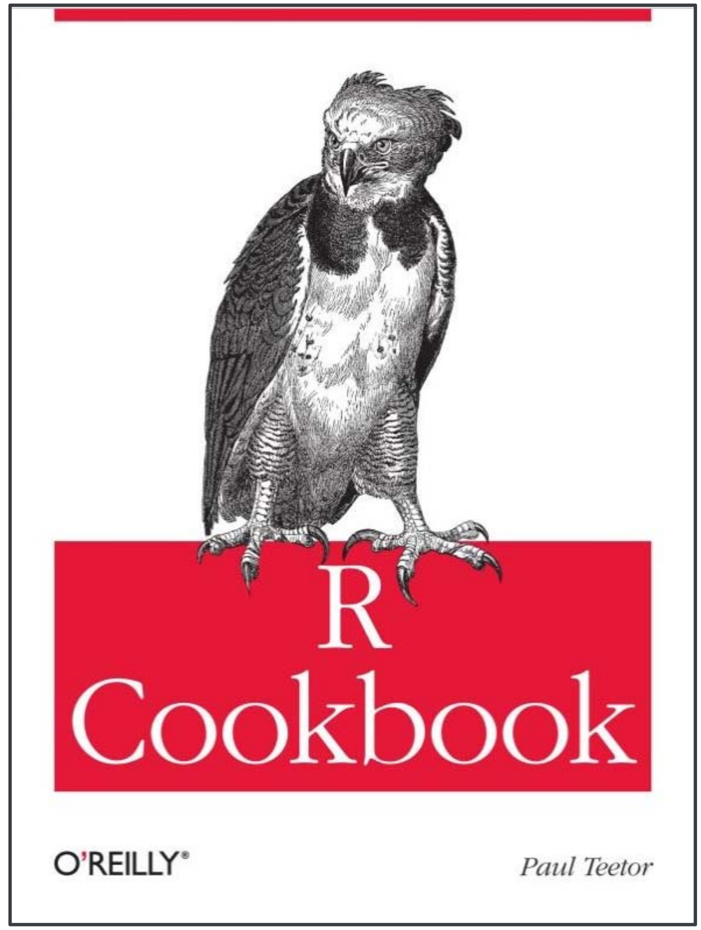


A couple of books you may like…





Summary

- Discoveries mostly use machine-learning methods
- You may like to learn a little R
- Deep-learning and spectral processing methods are part of ML
- Many models involve IoT and sensor-bearing wearables and telemetry
- Many models involve parsing of concepts from unstructured text
- ML models usually involve math (not IF-THEN rules or flowcharts)
- Relatively few involve conventional statistical ‘regression’ models
- All involve mapped ontology for discovery and operations
- PMML model standard for ‘open’ interoperability/portability
- Supervised automapping of ontologies, for model variables
- Regulatory and governance policies are evolving
  - 21^{st} Century Cures, FDA regulation, etc.

Summary (contin.)

- Health informatics: transformed by Big Data and New Data (IoT, etc.)
- Machine-learning and research: data-driven vs. hypothesis-driven
- Knowing ‘what,’ not ‘why,’ is sufficient to drive productive research
- Discovering patterns is within scope of CMIO role
- ‘Translational research’ is not just “bench-to-bedside”
- It is also translating the other direction: “bedside-to-bench,” ML from as-treated observational data
  - Discovering new screening, diagnostics, prognostics
  - From existing as-treated EHR-derived HIPAA-compliant de-identified Big Data
  - From new data (esp. ‘omics, wearable sensors)
- Technology architecture matters (including quantum computing)
- Not everything is ‘learnable’

Summary (contin.)

- CMIOs have previously been preoccupied with MU and other initiatives
- CMIOs are increasingly catalysts of, and advocates for, discovery, from secondary-use assented de-identified EHR data
  - “Top 2 tiers of Dr. Landa’s Maslow Triangle” (Esteem; Self-actualization)
- GCRC, IRB, DSMB, other roles in institutions
- Career paths in pharma and med dev industry
- Career paths in public health and govt policy

Thank you!