Statistical Methods for Real-Time Monitoring of Physical Disability in Multiple Sclerosis

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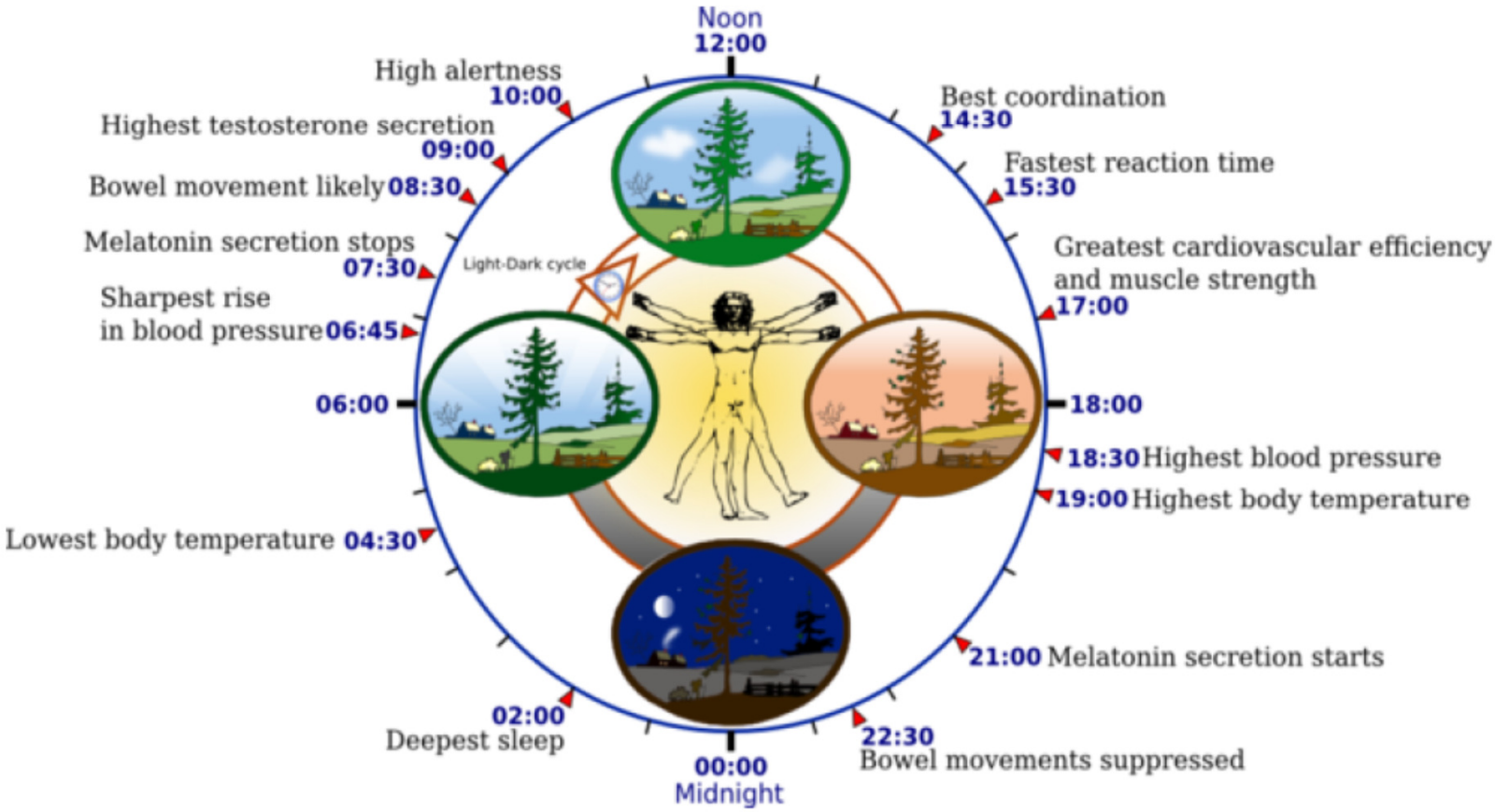
Actigraphy studies

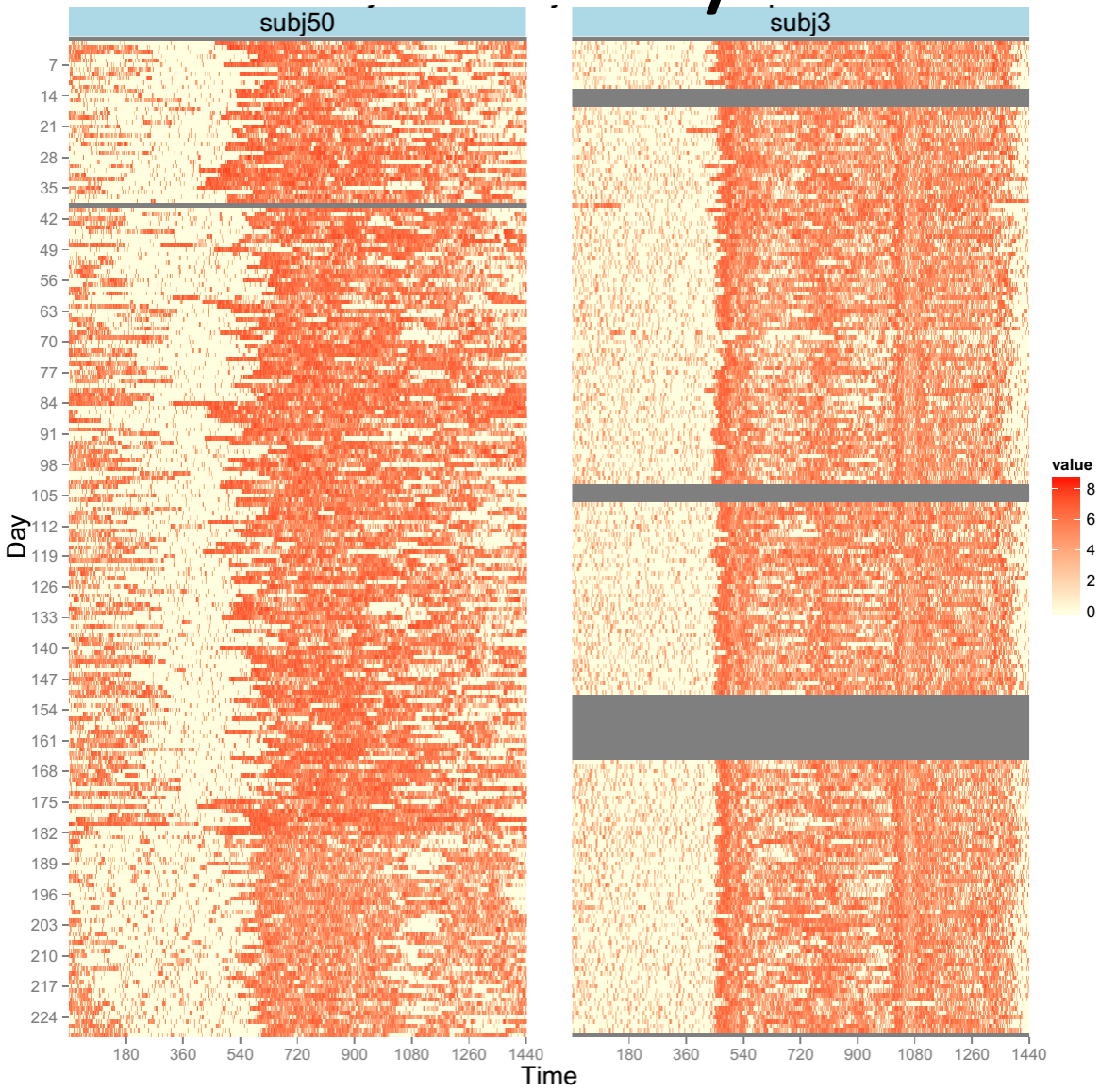
- Physical Activity and Aging
- Heart Failure Hospitalizations: real-time monitoring
- Aortic Valve Replacement: pre/post-operation
- Mental Health: Mood Disorders and EMA
- Physical Activity & Location (GPS)
- Parkinson Disease: cross-species studies
- Pediatric Surgery: early dispatch
- Sleep-wake vs Brain Atrophy & $A\beta$-amyloid




- Quantified-self (self-chronometry)



Stability/Disruptions in Circadian Rhythms



Wearables

Research





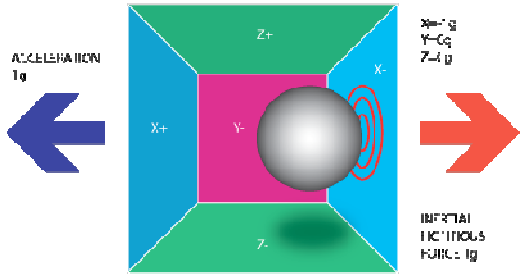
Consumer

What do research grade sensors offer?

- Dense measurements of Physical Activity
  - G's (mg)
  - Activity Counts (per minute)
  - Steps (per minute)
  - Gait (temporal gait asymmetry, stride variability)
  - Energy Expenditure (calories, …)
  - Sleep (duration, the number of wakes, …)
- Light, Temperature, others
- Heart Rate (ECG, BPM)
- Voice (Mood, Progression of Disease)
- App-based surveys (2-4 times a day)
- GPS

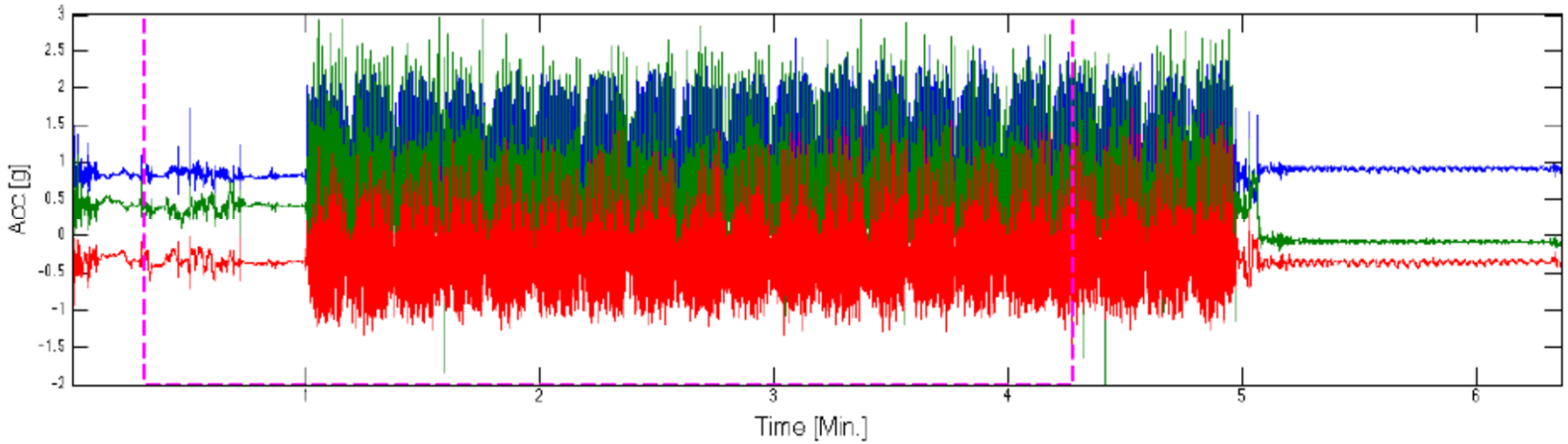
Accelerometers

- Use sensors to detect accelerations in one-to-three orthogonal planes
  - Anteroposterior
  - Mediolateral
  - Vertical



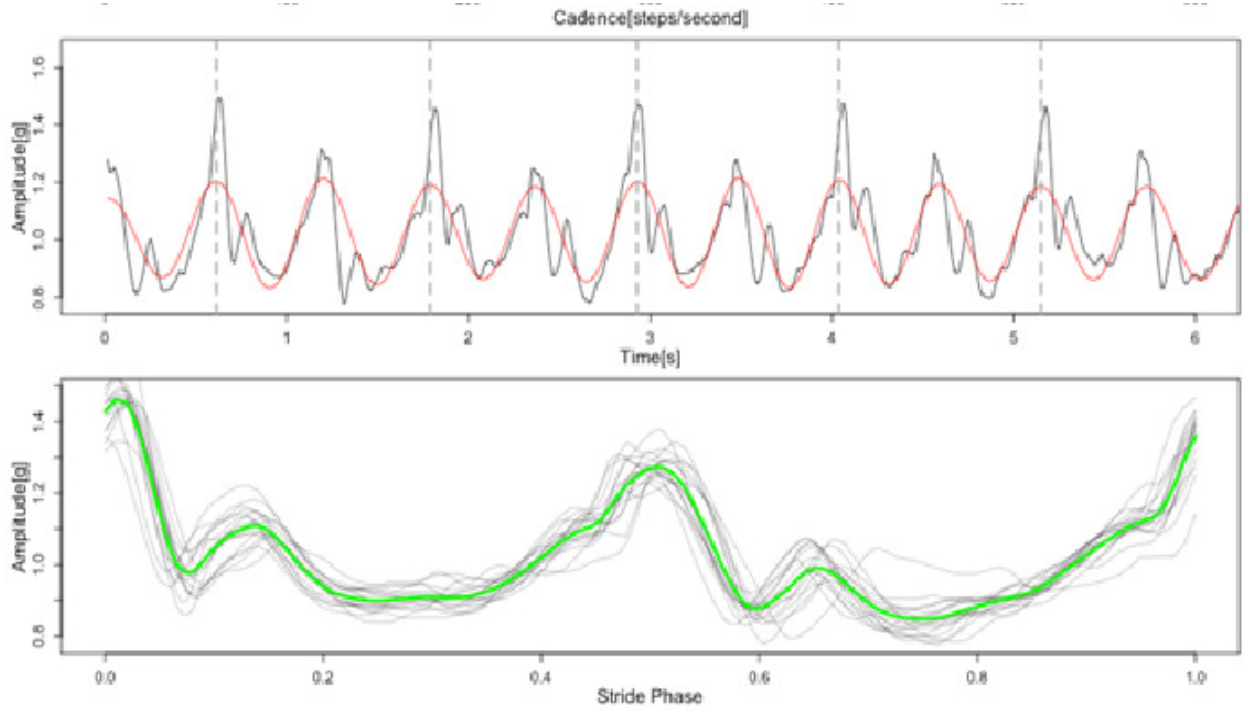
- Small size: wireless, non-invasive
- Long battery life, can record activity for up to 45 days (and down to 14 days)
- Provides an objective, comprehensive assessment of free-living physical activity

Value of the Raw data



- 400m walk: currently only time (gait speed)

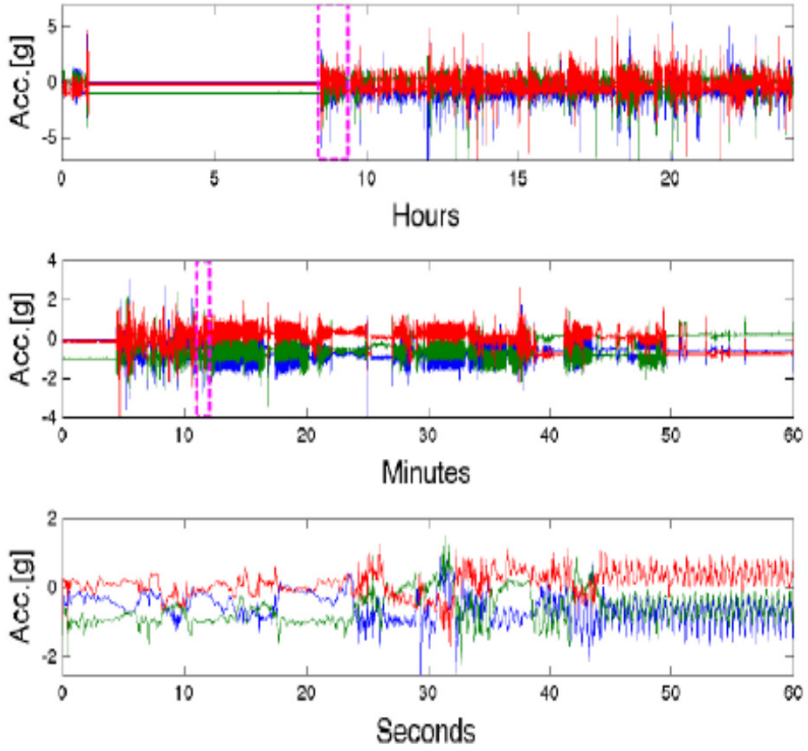
Temporal Gait Parameters

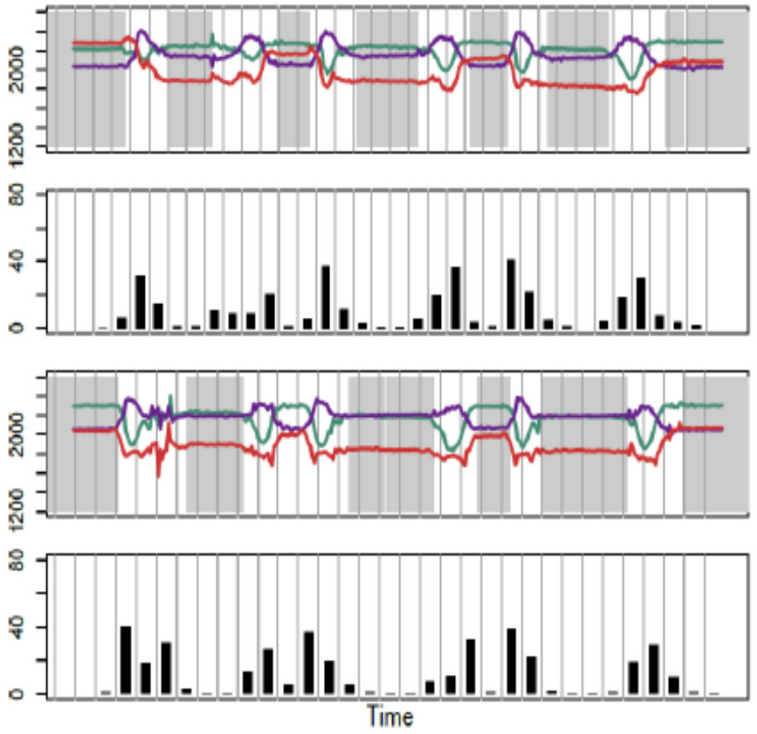


- quality of steps (AM vs PM)
- temporal gait parameters:
  - step asymmetry
  - stride variability
  - instantaneous walking speed

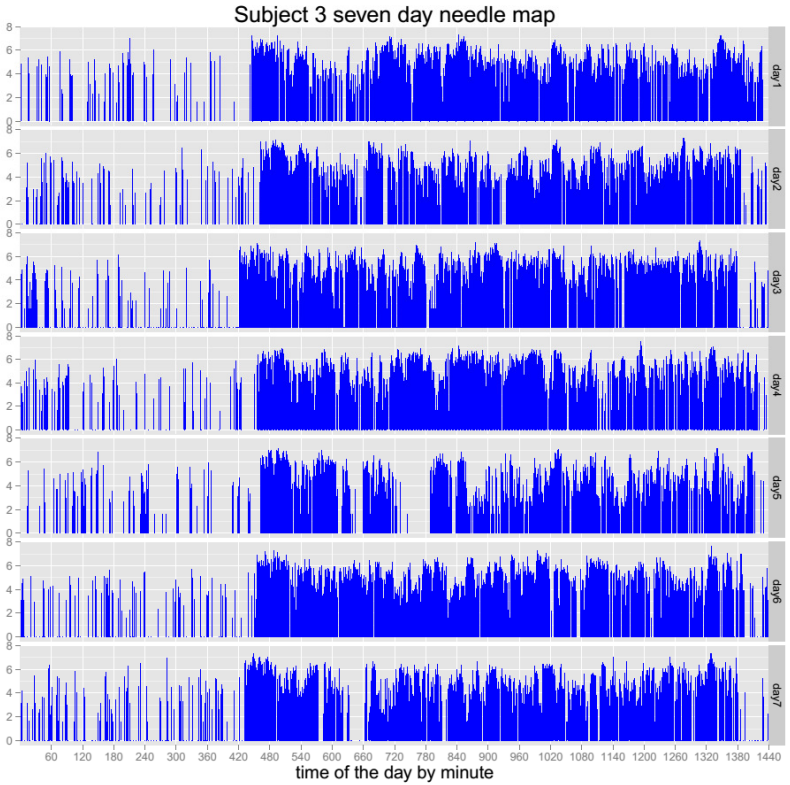
Urbanek, et al, arxiv.org

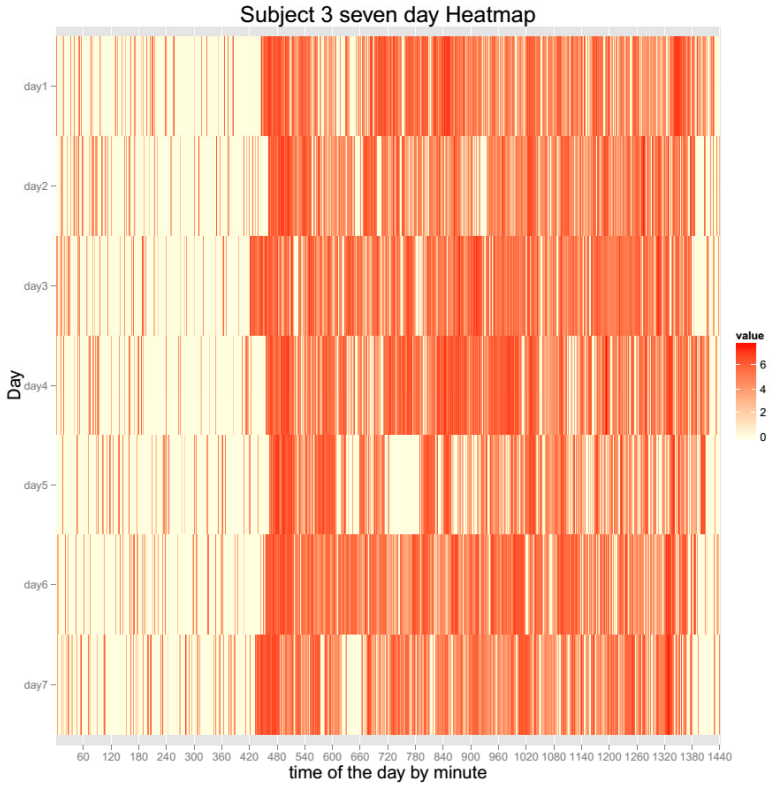
Minute-level activity count





Minute-level activity profiles





Epidemiological Studies and Clinical/Interventional Trials

- Epidemiological studies:
  - Cross-sectional/one visit: 7 -14 days per visit
  - Age, Sex, BMI,…
  - Nutrition, Heart Diseases, Mood Disorders, …

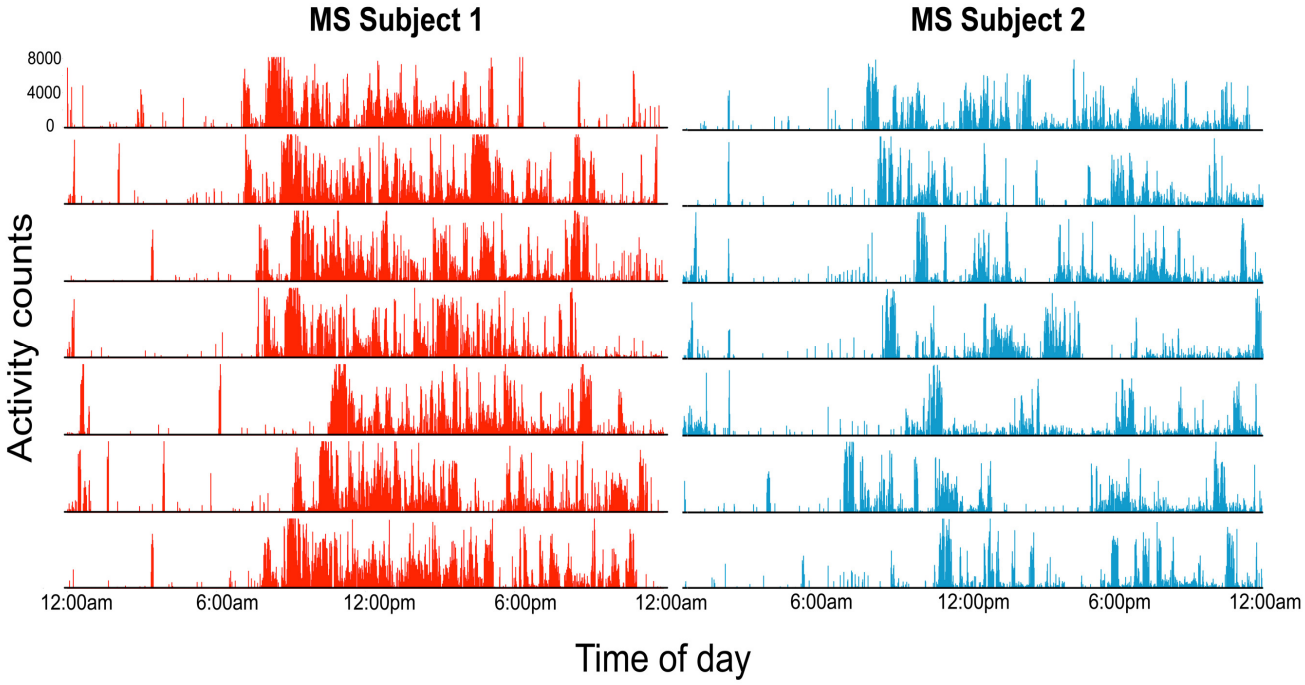
- Clinical trials:
  - two visits, multiple visits, continuous monitoring
  - mobile monitoring:
    - comparative effectiveness, pre-/post- intervention
    - progression, recovery
    - early detection (Congestive Heart Failure, Multiple Sclerosis)
  - part of the treatment
  - compliance to treatment
  - FDA: to define endpoints at Clinical Trial of 2020

Multiple Sclerosis (MS)

- Multiple Sclerosis
  - affects physical and cognitive function
  - slow accumulation of physical disability
- Expanded Disability Status Scale (EDSS)
  - non-linear scale
  - poor reliability and poor responsiveness
- **Our proposal:**
  - normalized physical disability score (real-life, accelerometry-based)

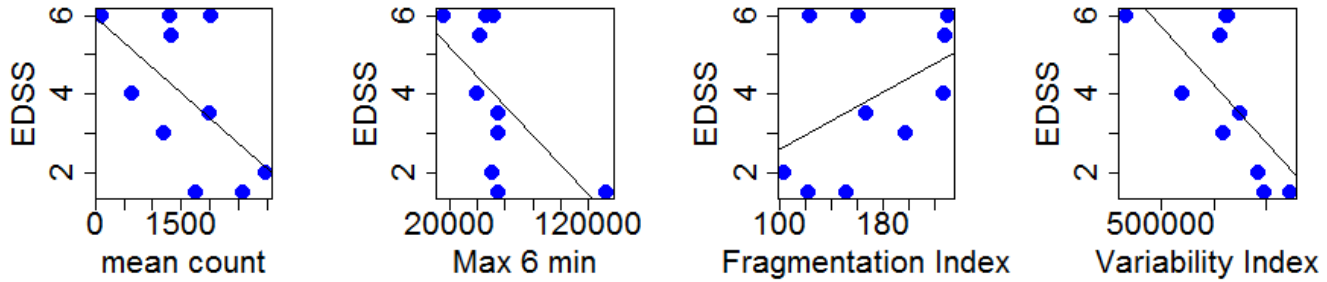
Preliminary Data

- Collected data on 10 subjects (1-7 days)
- Patient 1 (red) is a 61 year old female with an EDSS of 6.0
- Patient 2 (blue) is a 54 year old male with an EDSS of 4.0

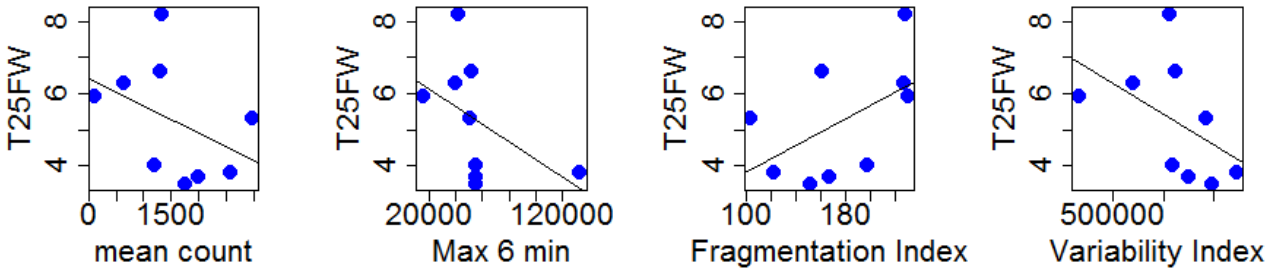


Preliminary Data

- Accelerometry vs EDSS

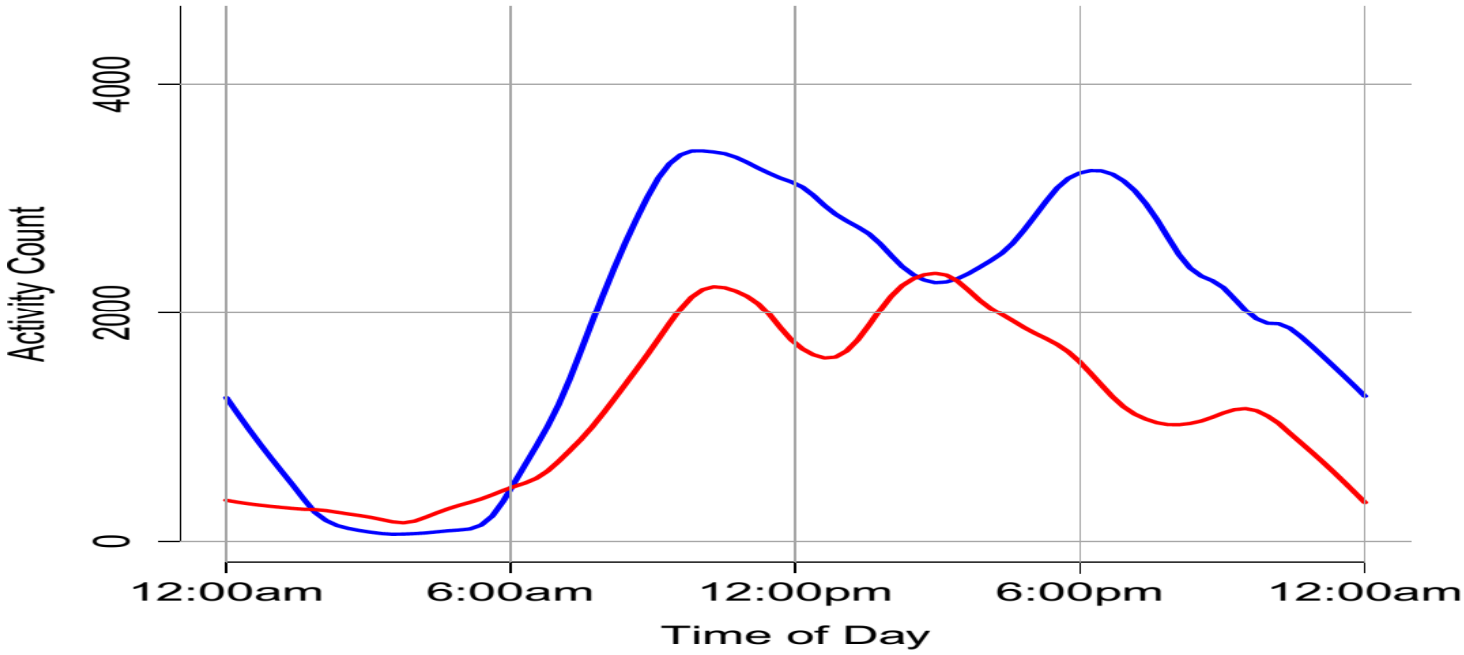


- Accelerometry vs t25fw



Preliminary Data

- Slow t25fw (red) vs Fast t25fw (blue)



Our approach

Step 1: Feature Extraction

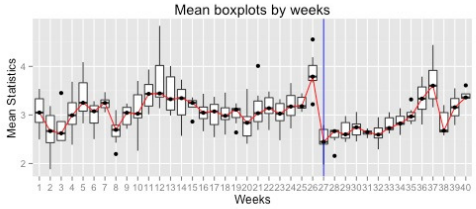
Step 2: Feature Selection

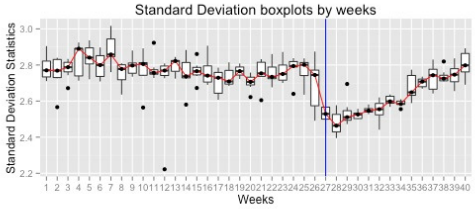
Step 3: Creating normalized physical-disability score

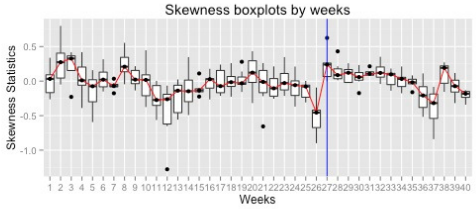
Step 1: Feature Extraction

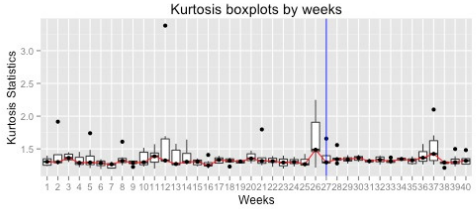
- Traditional time-invariant summaries (# of active minutes, total activity, max10, etc.)
- Time-dependent summaries (multiresolution: minute, hour)
- Temporal modeling of activity bouts (duration, frequency, magnitude), switching, fragmentation, stability/variability
- Temporal architercture of PA (functional PCs, landmarks of daily profiles)

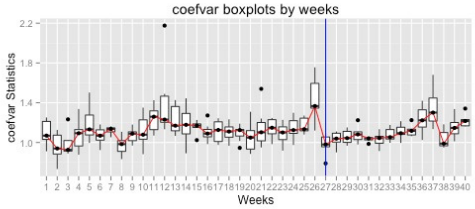
Step 2: Feature Selection

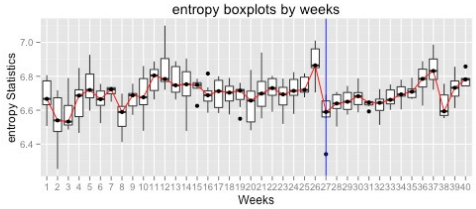


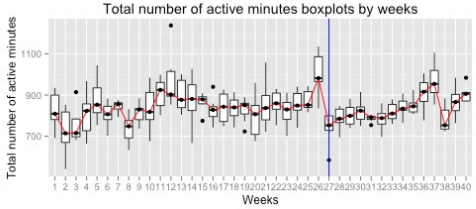


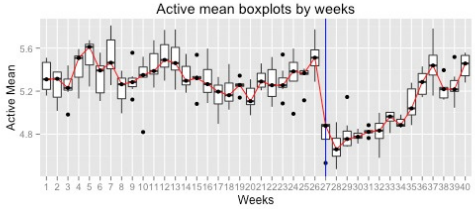


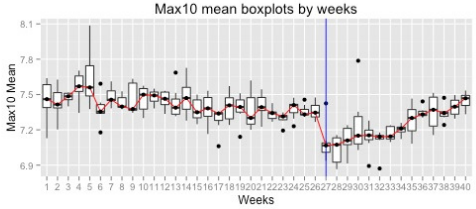


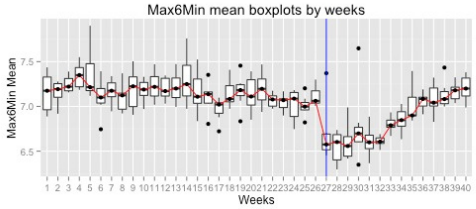


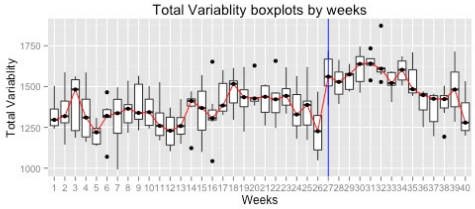


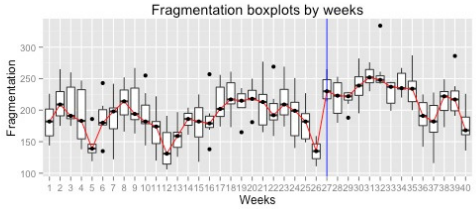




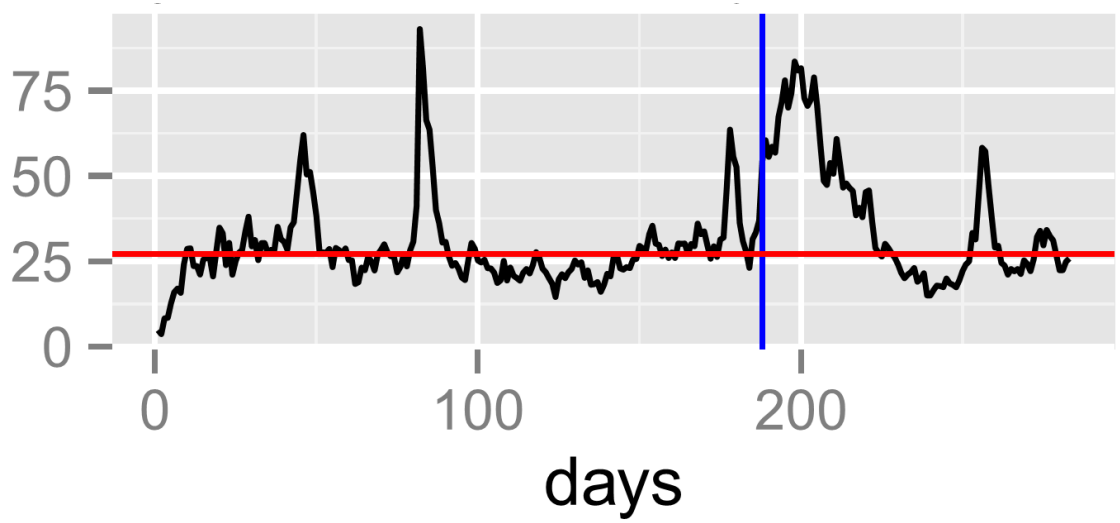








Step 3: Creating normalized physical-disability score



Zipunnikov, et al, unpublished data

Challenges

- Main Challenge: Steps 2 and 3

  - identifying features responsive to disability

  - no well-defined “events” (surgery/treatment, hospitalization)

Next Steps

- Collection data on 20 subjects (different levels of disability, 2 weeks each)
- Working out the main challenge