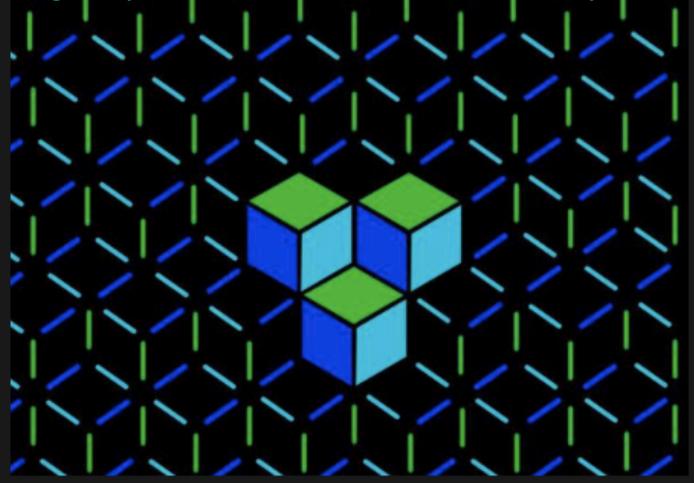# Opting out of existing Clinical Trials
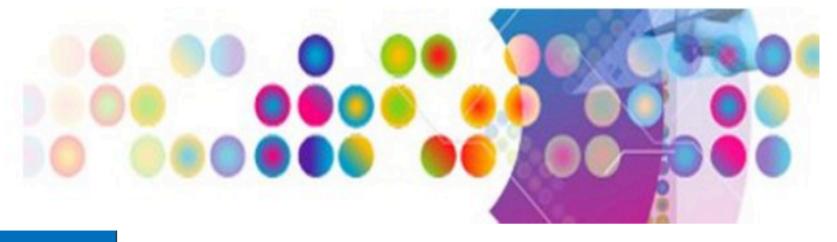# Knowledge experts, costs & benefits to society, who wins?

Open Sage Rally Sept 19, 2015

glance to the past

Sage Bionetworks Commons Congress 2010

PROGRAMS

Sage Commons Congress: Summary of Statements & Next Steps

our approaches

NASCENT TOOLS OF THE LAST DECADE

Now possible to generate massive amount of "omic's" data

Network Modeling Approaches for Diseases

IT Infrastructure and Cloud compute capacity allows
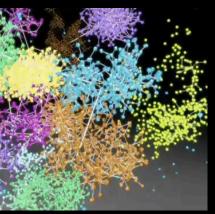a generative open approach to problem solving

Uncoupling the linkage between those that generate data and
those that analyze data

Nascent Movement for patients to generate and share data

Open Social Media allows citizens and experts to use gaming to
solve problems

STATE OF THE TECHNOLOGY

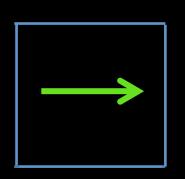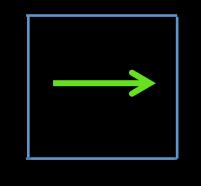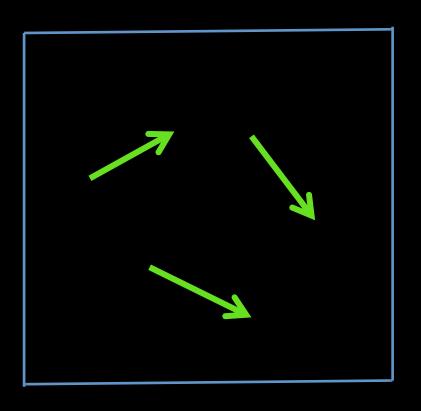STATE OF THE INSTITUTIONS

DISCONTINUITY

We focus on a world where **biomedical research** is about to fundamentally change. We think it will be often conducted in an **open, collaborative** way where **teams of teams** far beyond the **current guilds of experts** will contribute to making better, faster, relevant discoveries

github

PHILOSOPHICAL TRANSACTIONS:

GIVING SOME

ACCOMPT

OF THE PRESENT
Undertakings, Studies, and Labours
OF THE

INGENIOUS

IN MANY
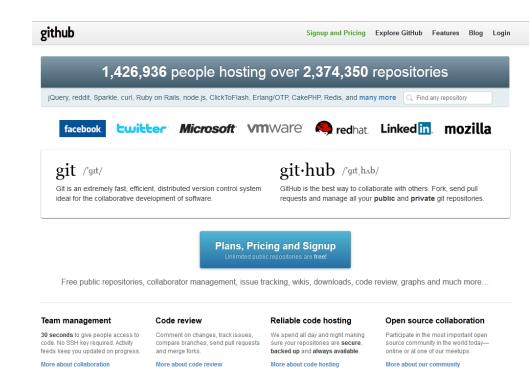CONSIDERABLE PARTS
OF THE

WORLD.

Vol I.

For Anno 1665, and 1666.

In the SAVOY,
Printed by T. N. for John Martyn at the Bell, a little with-
out Temple-Bar, and James Allestry in Duck-Lane,
Printers to the Royal Society.

Text summary of the completed project
Assembled after the fact

github

| Signup and Pricing | Explore GitHub | Features | Blog | Login |

1,426,936 people hosting over 2,374,350 repositories

jQuery, reddit, Sparkle, curl, Ruby on Rails, node.js, ClickToFlash, Erlang/OTP, CakePHP, Redis, and many more

Find any repository

facebook twitter Microsoft vmware redhat Linked in mozilla

git /'gɪt/

Git is an extremely fast, efficient, distributed version control system ideal for the collaborative development of software.

git·hub /'gɪt,hʌb/

GitHub is the best way to collaborate with others. Fork, send pull requests and manage all your **public** and **private** git repositories.

Plans, Pricing and Signup
Unlimited public repositories are **free!**

Free public repositories, collaborator management, issue tracking, wikis, downloads, code review, graphs and much more…

Team management
30 seconds to give people access to code. No SSH key required. Activity feeds keep you updated on progress.

More about collaboration

Code review
Comment on changes, track issues, compare branches, send pull requests and merge forks.

More about code review

Reliable code hosting
We spend all day and night making sure your repositories are **secure**, **backed up** and **always available**.

More about code hosting

Open source collaboration
Participate in the most important open source community in the world today—online or at one of our meetups.

More about our community

Every code change versioned
Every issue tracked
Every project the starting point for new work
All evolving and accessible in real time
Social Coding

Synodos / NF2

Progenitor Cell Biology Consortium

DREAM Challenges

Influenza Vaccinations

Psychosis Spectrum Disorder

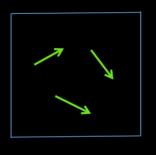Dengue Fever

CommonMind Consortium

Mozilla Science Labs

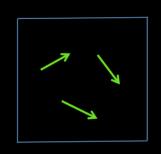Accelerating Medicines Partnership
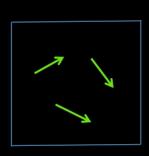
PsychENCODE

TCGA Pan-Cancer Consortium

CRC Subtyping Consortium
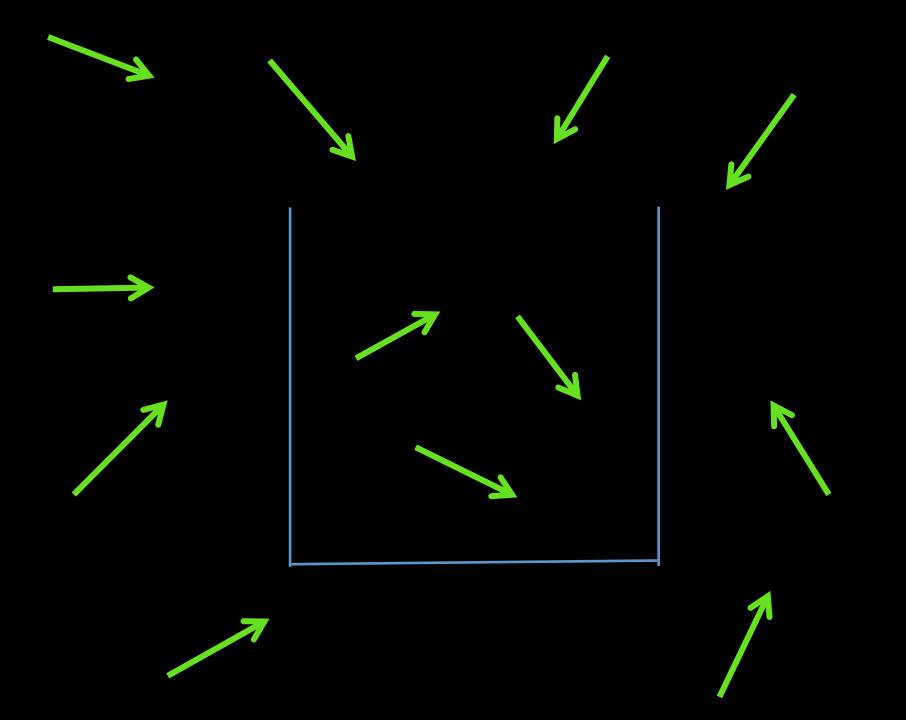
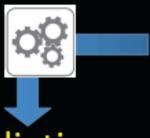Next Gen Scientific Publishing

Type II Diabetes

Structure of a Challenge
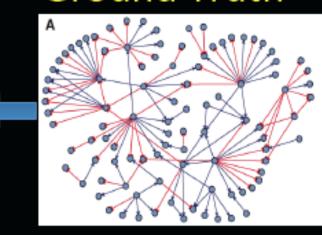
Incentivizing Continuous Participation

- Monthly leaderboard winners
  - Winner is highlighted within the Chal community
  - Winner posts a blog on winning
  model to Synapse

- Communities that link to the Leaderboard
  - Stackoverflow: Q&A site with 1,000,000 users
  - Science Translational Medicine community

Model From "Attractor Metagenes" Team Tops The September 1 Leaderboard!

SEPTEMBER 7, 2012 BY THEANORMAN (EDIT)

Please join all of us at DREAM and Sage Bionetworks in congratulating the "Attractor Metagenes" team for their September 1 Leaderboard Winner Achievement. Please read on to hear from Wei-Yi Cheng who submitted the winning model on behalf of his team. The BCC Support Support Team

Dear fellow BCC challenge participants and organizers,

This is Wei-Yi Cheng, along with my teammates Tai-Hsien Ou Yang and Professor Dimitris Anastassiou at Columbia University. It is our great honor to be highlighted as the top team on September 1st in the competition. Tai-Hsien and I are currently Ph.D. students in Prof. Anastassiou's Genomic Information Systems Laboratory (GISL) and the three of us have recently been working extensively to develop prognostic models in this challenge. I would like to thank the organizers for giving me the opportunity to present ourselves, and the ideas that we have been using.

stackoverflow   Questions   Tags   Users   Badges   Unanswered

Source only part of a file

Sage Bionetworks · DREAM   CONTRIBUTE to cancer research   Breast Cancer
COMPETE to publish your model   Challenge

3   My R workflow is usually such that I have a file open into which I type R commands, and I'd like to execute those commands in a separately opened R shell.

1   The easiest way of doing this is to say `source('the-file.r')` inside R. However, this always reloads the whole file which may take considerable time if big amounts of data are processed. It also requires me to specify the filename again.

Ideally, **I'd like to source only a specific line (or lines) from the file** (I'm working on a terminal where copy&paste doesn't work).

DREAM ALS Stratification
Prize4Life Challenge

- Data set is ready: fully harmonized clinical data set of >9,000 ALS patients
- Challenge objective: algorithms that can assist with stratification of ALS patient populations to help improve individual patient-level prognosis and to improve the success rate of clinical trials

glance to the future

The community that will lead in this new world will invest in places that can train those capable of solving dynamic complex multidimensional problems.

ways to allow individuals
Interested in health and disease
and other issues
to contribute their data and insights

allow those wanting to build out ways
to more easily collect
information and insights
using Federated Approaches
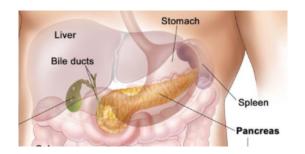(Open Source Sharing Code and Insights)

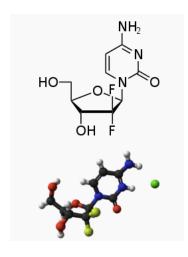self awareness

incentives and motivation

generosity

empathy

How big is the gap between clinical knowledge and clinical care?

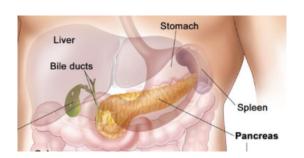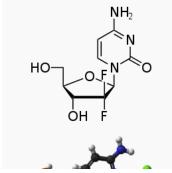# Consequences to society from the use of emerging solutions using pervasive computing devices

As with fluorouracil and other analogues of pyrimidines, the triphosphate analogue of gemcitabine replaces one of the building blocks of nucleic acids, in this case cytidine, during DNA replication. The process arrests tumor growth, as only one additional nucleoside can be attached to the "faulty" nucleoside, resulting in apoptosis.

As with fluorouracil and other analogues of pyrimidines, the triphosphate analogue of gemcitabine replaces one of the building blocks of nucleic acids, in this case cytidine, during DNA replication. The process arrests tumor growth, as only one additional nucleoside can be attached to the "faulty" nucleoside, resulting in

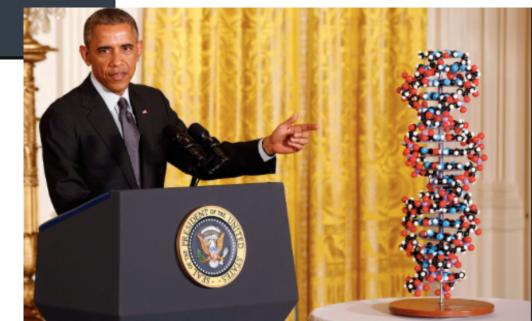| Mutated Genes					Copy Number Altered Genes				
Gene	# Mut	Samples	Freq		Gene	Cytoband	CNA	Samples	Freq
TP53	23	23	85.2%		MECOM	3q26.2	AMP	8	29.6%
PIK3CA	14	12	44.4%		KAT6A	8p11	AMP	7	25.9%
TTN	6	5	18.5%		MYC	8q24.21	AMP	6	22.2%
ARHG...	5	5	18.5%		MUC1	1q21	AMP	6	22.2%
CSMD3	5	5	18.5%		ASXL1	20q11	AMP	6	22.2%
DMD	4	4	14.8%		POFUT1	20q11	AMP	6	22.2%
PPP2...	4	4	14.8%		CCNE1	19q12	AMP	6	22.2%
USH2A	4	4	14.8%		ERBB2	17q12	AMP	6	22.2%
FBXW7	4	4	14.8%		ARFRP1	20q13.3	AMP	6	22.2%
PTEN	5	4	14.8%		TP63	3q28	AMP	6	22.2%

Second-generation antipsychotic agents

Efficacy There have been numerous double-blind studies comparing the efficacy and tolerability of SGAs with FGAs for acute and maintenance therapy for schizophrenia. Such an expansive review is, however, beyond the scope of this paper; thus, the reader is referred to other sources.[1, 5, 152] In general, although the proportion of patients who improve and the magnitude of therapeutic effects vary greatly, SGAs appear to be at least as effective for psychotic symptoms as FGAs (for reviews, see Markowitz *et al*[153] and Remington and Kapur[154]). However, there has been considerable debate with regard to the clinical superiority of SGAs over FGAs.
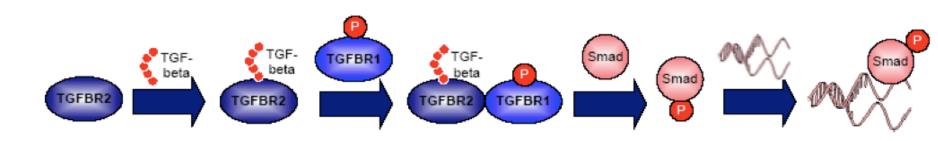
Geddes *et al* conducted a systematic review and meta-analyses of 52 randomized trials comparing new antipsychotics (clozapine, olanzapine, risperidone, quetiapine, sertindole and amisulpride) with FGAs (haloperidol or chlorpromazine).[155] There was no difference in efficacy between FGAs and SGAs, in trials that used a dose of an SGA in haloperidol equivalents of 12 mg/day or less. For example, the

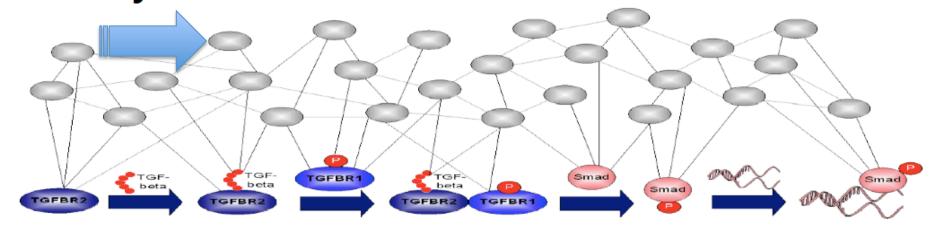# Current status of Precision Medicine Initiative and omics driving decisions
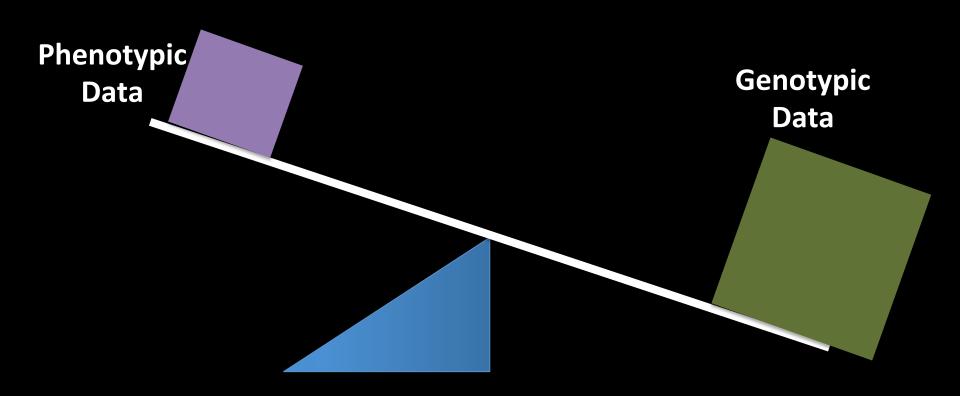
The way we like to think:

The way it is:

(Eric Schadt)

Asymmetry of Data:
The public can help with this

Phenotypic Data

Genotypic Data

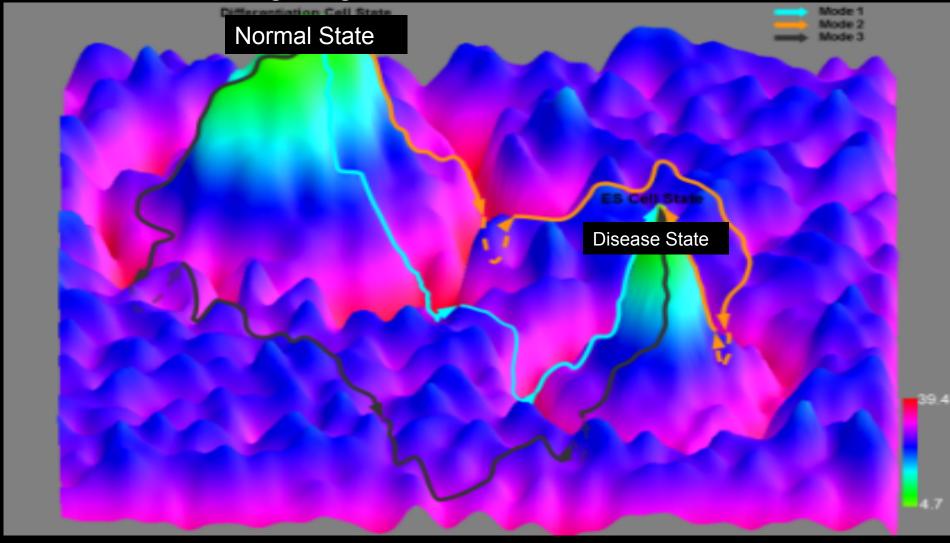Current Clinical Understanding as driven by Clinical Trials

Carried out using clinician's time with data owned by Institutions

Usually collected using crude categories

Pen and paper subjective surveys

Siloed by Consents restricting sharing data

Navigating between states of wellness

We need to fundamentally change the current approaches

N

T

D

M

How smart phones as pervasive computing devices help

Jon Berkeley

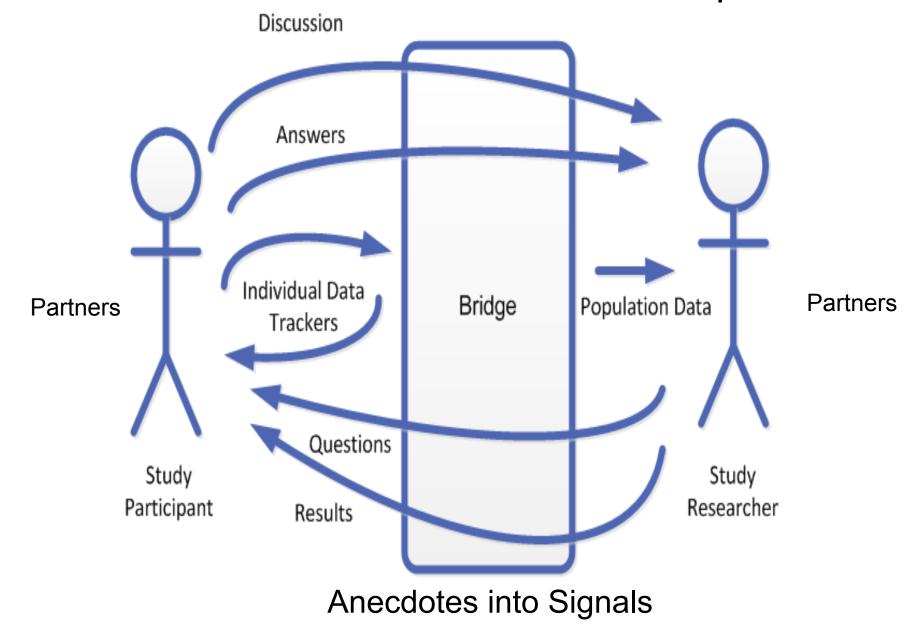| Current Measures	Smartphone Measures
Insensitive	Sensitive
Subjective	Objective
Episodic	Continuous
Provider-Centered	Individual-Centered
In Clinic	Remote
Unidimensional	Multidimensional
Limited Feedback	Real-time Feedback

BRIDGE

Incorporating open data, patient wisdom and public involvement into biomedical research

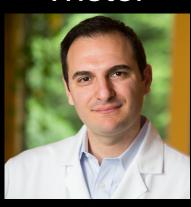# Participant –Centered Research Studies with Feedback Loops

Discussion

Answers

Partners

Individual Data Trackers

Bridge

Population Data

Partners

Study Participant

Questions

Results

Study Researcher

Anecdotes into Signals

mHealth   Research Kit
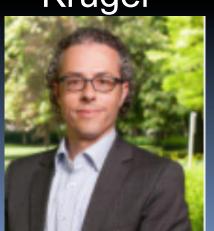
Dorsey

Trister

Klein

mPower

Kieburtz

Tanner

Kruger

Bloem

James Parkinson, 1817

AN

ESSAY

ON THE

SHAKING PALSY.

BY

JAMES PARKINSON,
MEMBER OF THE ROYAL COLLEGE OF SURGEONS.

LONDON:
PRINTED BY WHITTINGHAM AND ROWLAND,
Goswell Street,

FOR SHERWOOD, NEELY, AND JONES,
PATERNOSTER ROW.

1817.

"Involuntary tremulous motion, with lessened muscular power, in parts not in action and even when supported; with a propensity to bend the trunk forward, and to pass from a walking to a running pace: the senses and intellects being uninjured."
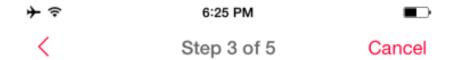
Original scientific questions from mPower

- Feasibility of using apps to reliably track real-time information in PD

- Are there real day-to-day and week-to-week variations in PD that provide valuable opportunities for intervention?

- Do remote sensor data allow for unpacking of symptoms?

- Can multidimensional tracking from remote sensor data enable more sensitive descriptions of personalized symptoms in those with PD?

- Can we measure the effects of modulators like medications, sleep and exercise on these day-to-day and week-to-week variations?

Tracking four key symptoms of PD using Surveys - Structured Activities - Passive Measurements

	Motor Initiation	Gait/Balance	Hypophonia	Memory
Passive	GPS - Displacement Vectors	GPS - Displacement Vectors	-	-
Structured Activity	Tapping Activity	Walking Activity	Voice Activity	Memory Game
Surveys	MDS-UPDRS PDQ8	MDS-UPDRS PDQ8	MDS-UPDRS PDQ8	MDS-UPDRS PDQ8

* All structured activities also include timing with relation to med administration

Component	Data Feed	Features
Walking/Standing/Turning	x,y,z,q sampled at 10 Hz (all) magnetic field, rotation, gravity (M7/8)	vectors of motion to measure sway, ultimately amplitude to step
Voice	5 second m4a recording background 10 second m4a recording phonation	characteristics of amplitude, jitter, frequency, etc
Tapping	timestamp, x, y for 20 seconds, accelerometer at 10 Hz	standard statistics, second order features
Memory Game	overall score	score
GPS Displacement	q10 minute vector (distance, direction)	random walks
MDS-UPDRS	Likert 0-4 answers to 16 questions	Scores
PDQ-8	Likert 1-5 answers to 8 questions	Scores

Parkinson mPower Study App

Tapping Interval Test

Rest your phone on a flat surface. Then use two fingers on the same hand to alternately tap the buttons that appear. Keep tapping for 20 seconds and time your taps to be as consistent as possible.
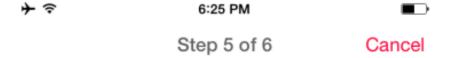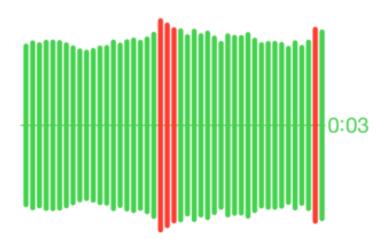
Tap Get Started to begin the test.

App launched on 3/9
Ray Dorsey, U Rochester

Scientific Advisors
- Karl Kieburtz, U Rochester
- Caroline Tanner, UCSF
- Bas Bloem, Radboud U
- Max Little, Aston U
Foundation Partners
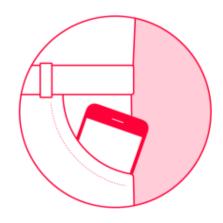- Michael J Fox Foundation
- ParkinsonNet

Parkinson mPower Study App

Step 5 of 6　　　Cancel

Say "Aaaaah" into
the microphone for
as long as you can.

0:03

Parkinson mPower Study App

Parkinson mPower Study App
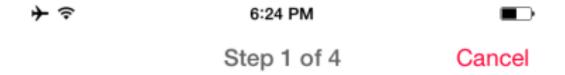
Spatial Memory Test

This test measures your spatial memory by showing you patterns and asking you to recall and repeat them.

In 6 months since launch on March 9, 2015

- 59,700 downloads from app store

- 16,585 participants consented (28% of total downloaded)

- 15,185 participants enrolled (92% of all consented)

- 17% of participants who completed enrollment survey indicate a diagnosis of Parkinson disease (1501/8715)

- Share the data

Sharing Options

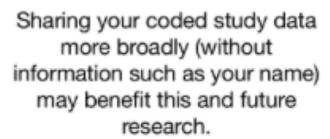Stanford will receive your study data from your participation in this study.

Sharing your coded study data more broadly (without information such as your name) may benefit this and future research.

Learn more

Share my data with Stanford and qualified researchers worldwide ›
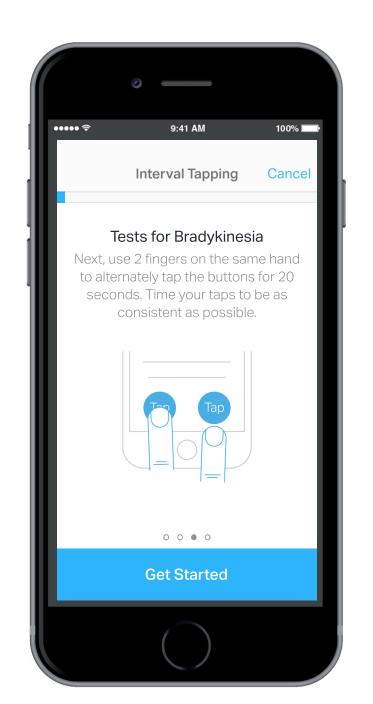
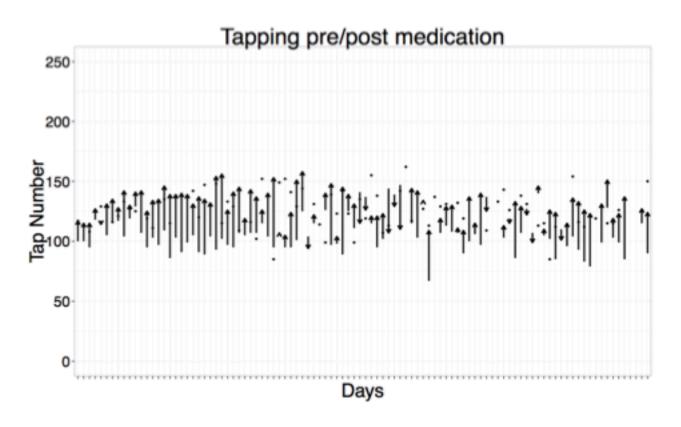Only share my data with Stanford ›

Sent from Stephen's iPhone

Total volume of data

In the six months since mPower was launched, the 1501 PD patients enrolled would have had:

	Frequency	Observations
Physical examination	q2months	60
Observational research	weekly	1,056
mPower	daily/continuous	452,105
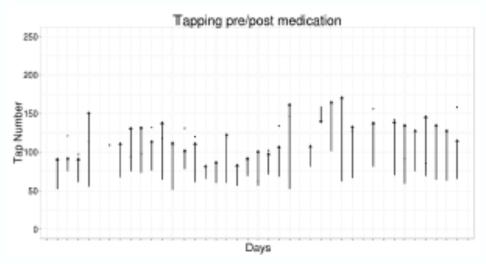
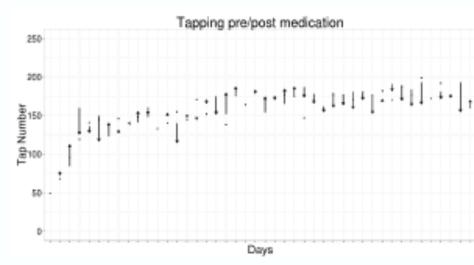# Longer term data shows changes in the pattern of effects of medication in an individual

Tapping pre/post medication

New measures of PD:
Benefits of unpacking the dimensions of tapping

Traditional Measures	First-order Features
Number of Taps	Number of taps, Mean tapping interval, Median tapping interval, Minimum tapping interval, maximum tapping interval, Standard deviation of tapping interval, Kurtosis of tapping interval, Interquartile range of tapping interval, Interquartile range of right button X, Range right button X ,Standard deviation right button X, Interquartile range of left button X, Range left button X ,Standard deviation left button X, Interquartile range of right button Y, Range right button Y ,Standard deviatiion right button Y, Interquartile range of left button Y, Range left button Y ,Standard deviation left button Y, Correlation X and Y, Skew tapping interval, No-button tapping frequency

Personalized approaches to unpacking multidimensional data from remote sensors

62 year old man
2009 Onset of Symptoms / Start meds
Mean change: 51 taps
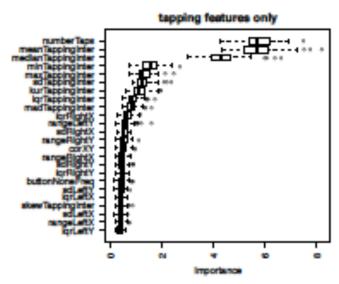Max change: 111 taps
Min change: -21 taps

67 year old woman
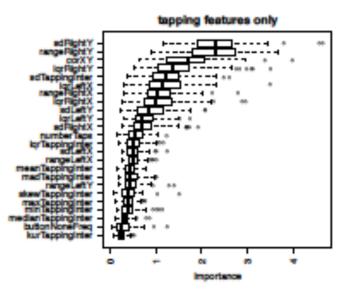2004 Onset of Symptoms / 2009 meds
Mean change: -4 taps
Max change: 28 taps
Min change: -38 taps

Different features are important to predict effect of medications for different patients

Number of Taps
Mean Tapping Interval
Median Tapping Interval

Standard Deviation R Y
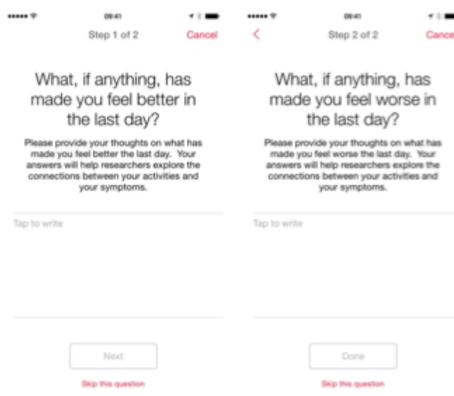Range Right Y
Correlation X Y

Role of empowering participants- Interventions

Because mPower enables realtime assessments of both symptoms and modulators there is an opportunity to identify windows of intervention

Symptoms

	Motor Initiation	Gait/Balance	Hypophonia	Memory
Passive	GPS - Displacement Vectors	GPS - Displacement Vectors	-	-
Structured Activity	Tapping Activity	Walking/standing Activity	Voice Activity	Memory Game
Surveys	MDS-UPDRS PDQ8	MDS-UPDRS PDQ8	MDS-UPDRS PDQ8	MDS-UPDRS PDQ8

Modulators

Is there evidence of modulators beyond medications?

- 5,192 unique participants provided 17,076 responses to questions about what made them feel better or worse on that day

Examples of Better:
"I went to visit with family that made me feel better"
"Sinemet and lying down for an hour in the afternoon."
"Laying down"
"The sun starting to come out in the warmth of the day because were entering spring"
"I got some really good news about a stray cat of the nursing back to health."
"Meetings"
"Computer games"
"Completing a list of tasks for daily activities"
"Looking for furniture for my new house"
"Practicing Zen Meditation!"

Examples of Worse:
"Walking"
"Not getting a good nights sleep the night before"
"I don't think anyone in my family really understands what Parkinson's disease is and how it is impacting my life and my work."
"Worrying that I not getting things done around the house"
"Having a glass of wine"
"Nothing"
"Sadness regarding race relations in America!"
"Getting comfortable sleeping. Keep moving my sleeping position which leads to restless night."

How can mPower impact clinical practice?

| Diseases as syndromes | → | Diseases as clusters of symptoms | → | Diseases as clusters of specific features |

Anticipating an inevitable transition that underlies the concept of precision medicine

James Parkinson, 1817

AN

ESSAY

ON THE

SHAKING PALSY.

BY

JAMES PARKINSON,
MEMBER OF THE ROYAL COLLEGE OF SURGEONS.

LONDON:
PRINTED BY WHITTINGHAM AND ROWLAND,
Goswell Street,

FOR SHERWOOD, NEELY, AND JONES,
PATERNOSTER ROW.

1817.

"Involuntary tremulous motion, with lessened muscular power, in parts not in action and even when supported; with a propensity to bend the trunk forward, and to pass from a walking to a running pace: the senses and intellects being uninjured."

PD Clinical Features, 2008

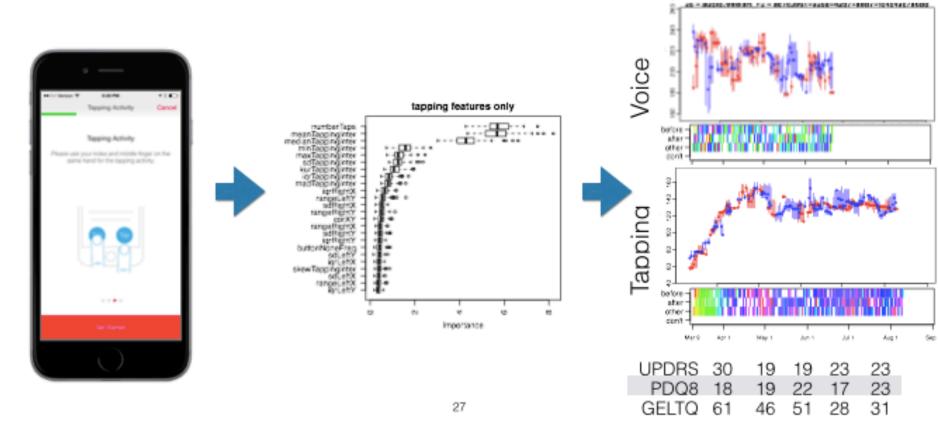|	
Tremor, bradykinesia, rigidity, postural instability	Cognitive impairment, bradyphrenia, tip-of-the-tongue (word finding) phenomenon
Hypomimia, dysarthria, dysphagia, sialorrhoea	Depression, apathy, anhedonia, fatigue, other behavioural and psychiatric problems
Decreased arm swing, shuffling gait, festination difficulty arising from chair, turning in bed	Sensory symptoms: anosmia, ageusia, pain (shoulder, back), paresthesias
Micrographia, cutting food, feeding, hygiene, slow activities of daily living	Dysautonomia (orthostatic hypotension, constipation, urinary and sexual dysfunction, abnormal sweating, seborrhoea), weight loss
Glabellar reflex, blepharospasm, dystonia, striatal deformity, scoliosis, camptocormia	Sleep disorders (REM behaviour disorder, vivid dreams, daytime drowsiness, sleep fragmentation, restless legs syndrome)

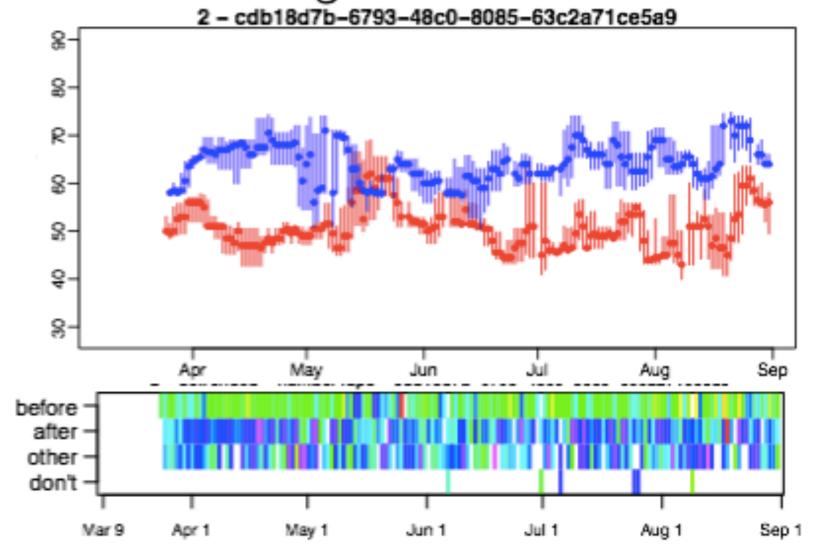Straw man proposal for a novel scorecard that yields a sensor-
based phenotype to allow for clinical tracking of features

UPDRS	30	19	19	23	23
PDQ8	18	19	22	17	23
GELTQ	61	46	51	28	31

mPower scorecard enabled dialogue with physician

Interesting examples from tapping:
Clear change with medication
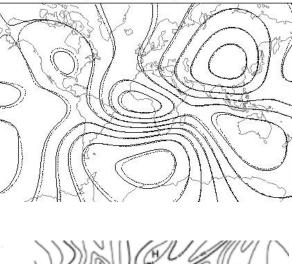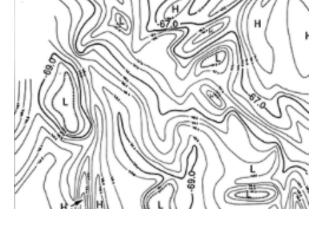

2 – cdb18d7b–6793–48c0–8085–63c2a71ce5a9

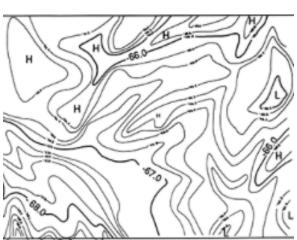Precision Medicine has up till now primarily focused on defining subgroups

It has not focused on realities of fluctuations

Hypothesis: Better tracking of patients at baseline and understanding the fluctuations in daily changes will allow more accurate measures of interventions
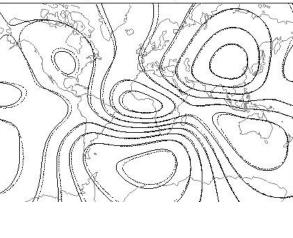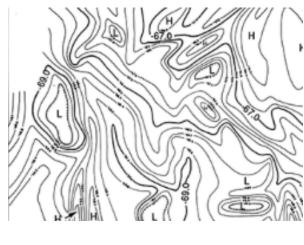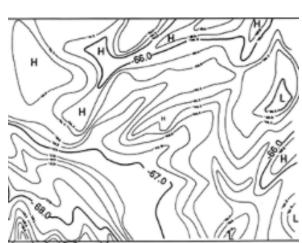Especially for changes in their quality of life

Opportunities for Pervasive Computing
  to impact Clinical Trials:

A. Pre-Enrollment baselines for patients
     before they enter trials

B. New secondary end-points and ways to
     distinguish from existing therapies

C. Post- Approval Surveillance
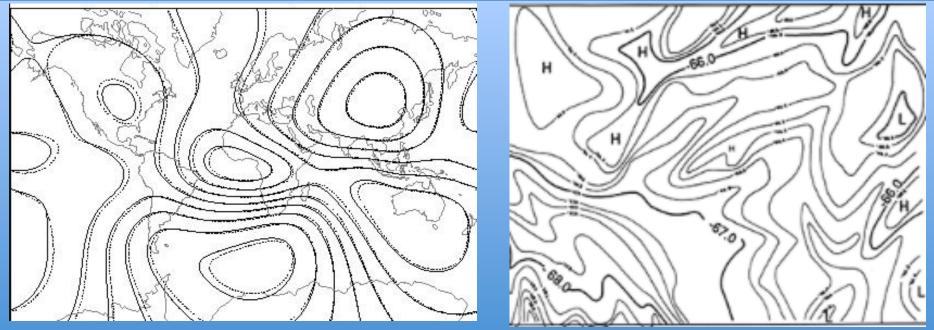
App-enabled trial participation: Tectonic shift or tepid rumble?

CLINICAL TRIAL CONUNDRUM

Much of our understanding of the effects of modulators (such as drugs) on human diseases comes from clinical studies. Today, tens of billions of dollars are spent on clinical trials that range from large longitudinal observational studies to intensive testing of potential new drugs. Trials are typically coordinated through physicians at specific institutions and

imagine a role for "actionable phenotypes"
potentially enriched by linking to genotypes

found in common in some individuals across diseases

indications for therapies and interventions
not bounded by a disease designations
approvals from FDA for improving quality of life

currently designing how we might assess
all > 200 primary movement disorders

(talk to Annett Bakker about the long tail in rare diseases

Paging Dr. Watson? IBM opened a new business center in Cambridge, Massachusetts to push its Watson Health initiative.

IBM's new Watson health building in Cambridge, Massachusetts.

IBM

IBM Watson Health Announces New Partnerships, New Cloud Services and Global HQ in Cambridge, MA

With the opening of the IBM Watson Cloud Health global headquarters in Cambridge, **IBM and Sage Bionetworks announce they will jointly develop an open biomedical research platform, comprising Sage's Bridge Server and Synapse technologies powered by the IBM Watson Health Cloud and associated analytics.** The platform will feature the IBM Watson Health Cloud as a preferred cloud provider on which Sage and other research teams can aggregate, store, curate, and analyze data collected via Apple ResearchKit apps. Sage currently has active ResearchKit projects in breast cancer and Parkinson's Disease. Further, Sage and IBM will collaborate to integrate the IBM Watson Health Cloud with Sage's BRIDGE server and Synapse, an informatics platform dedicated to supporting the large-scale pooling of data, knowledge, and expertise across institutions to solve some of the most challenging problems in biomedical research. Sage endeavors to engage patients in the scientific discovery process and facilitate global collaboration among researchers working toward a shared goal of advancing and accelerating medical research.

OPEN BIOMEDICAL RESEARCH PLATFORM

#NotatSage

#NotatSage

#NotAtSage

Digital information should trump classic "tragedy of commons"

(issues of scare resources)

and yet

Will the new digital commons be crushed by
the new tragedy of digital commons

Sequestering data that could flow

locked up by first mover "quasi-monopoly" information empires

Google, Facebook etc….

THE

MASTER

SWITCH

THE RISE AND FALL OF INFORMATION EMPIRES

TIM WU

compare and contrast

Generative open system of a health information commons
Acting as a "Biomedical Knowledge expert"

vs

one run as a quasi-monopoly

When will cost/benefit to society occur?

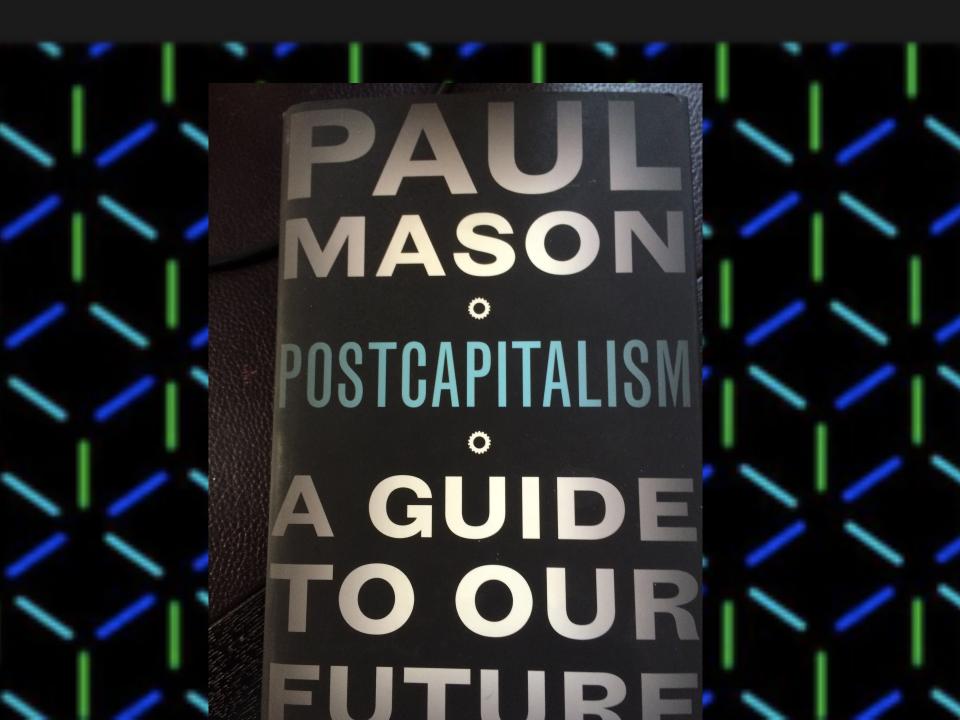so then what is needed

What sort of movement?

In 09' as beautifully stated by a doctor:

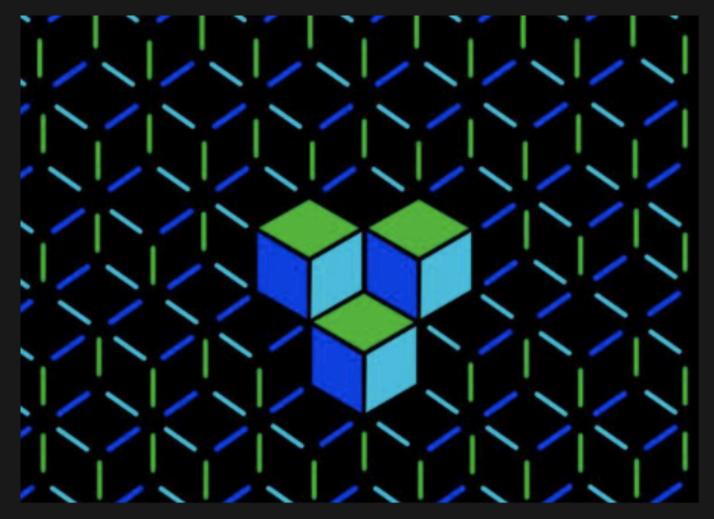"a postcapitalist society would have to be
a knowledge society"

"a new citizen culture must be disseminated among the public
A citizen science developed"

"

Alexander

Bogdanov

PAUL MASON

⚙

POSTCAPITALISM

⚙

A GUIDE
TO OUR
FUTURE

Sage Assembly March 25-27 2016 Shenzhen China

know thyself, know your home in the digital age