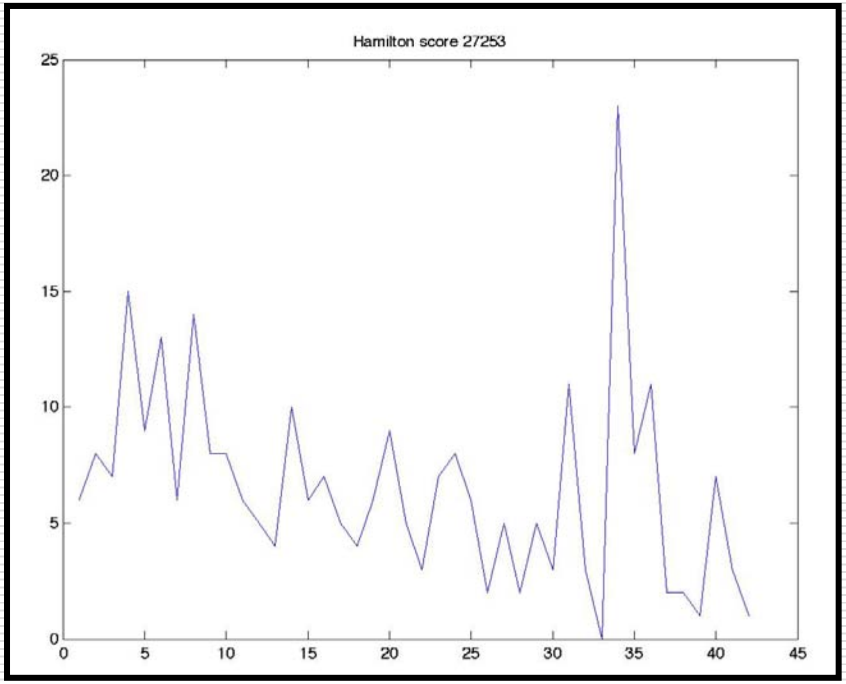
Modeling the dynamics of patients with bipolar disorder

Nicole Kennerly
NSF-NIH BBSI 2006
Mentor: Shlomo Ta'asan



Bipolar disorder, a.k.a. manic depression

- Characterized by abnormal brain functioning that results in severe changes in mood, energy, and performance[1]
- Sixth most disabling illness worldwide according to the World Health Organization[2]
  - Emotional effects
    - Often damages relationships, career, and day-to-day life
    - One in four of untreated cases ends in suicide[3]
  - Economic effects
    - Lost employment and productivity
    - High health and social care costs[4]

Why try using mathematical models to help bipolar patients?

- Successful treatment by other means has evaded psychiatrists for years
  - Bipolar illness is a symptom, not the cause
  - Helpful medicines vary from patient to patient

- Novel *in silico* approach
  - A new way of approaching many data that psychiatrists may have trouble interpreting
  - Practical Aspects
    - Estimation of parameters using clinical data
    - Translation of clinical questions into mathematical problems
  - Alter parameters or noise to reflect several factors, if necessary
    - Age, gender, nature of cycling

Objectives

- To develop a quantitative understanding of the illness
- To develop predictors for patient’s outcome based on a small amount of data points

Summer research outline

- Develop patient simulations
- Characterize the noise
- Add medicines to patient charts
- Parameter estimation

What can our mathematical model tell us about a bipolar patient?

Clinical Question → Math solution

- Is a treatment helping or is the patient doing worse?
- If a treatment is working, how long will it take for remission?
- What is the expected time for the next big episode?
- Which treatment (choice and dose) works best for a patient?

Construction of the model

- Define the minimum number of patient-dependent parameters that describe the time evolution of patient illness-index (2)
- Select equation type (stochastic differential equation)
  - Noise
  - Time
- Use clinical data to estimate the model's patient-dependent parameters
  - 10 years of data for 175 patients from Western Psychiatric Institute and Clinic
    - Hamilton score - measures depression
    - Young score - measures mania
- Employ MATLAB to analyze and visualize data

A stochastic model with two parameters

Assumption: The illness can be characterized with two (constant?) patient-dependent parameters.

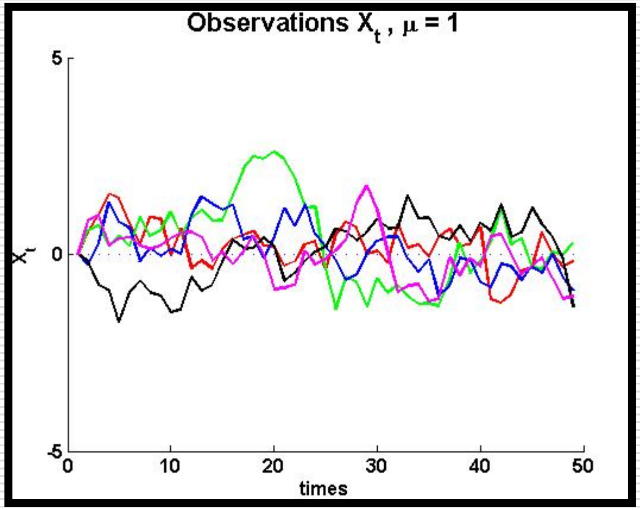
Analogy: The stock market model

$$\Delta x = -\mu x \Delta t + \sigma \Delta L$$

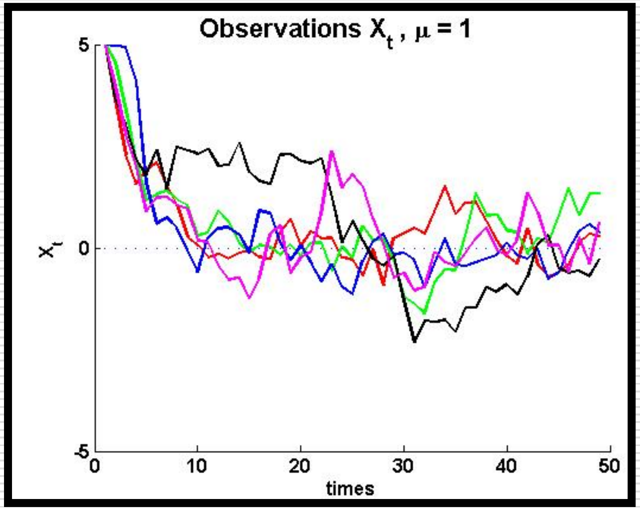
		μ		σ
Change in illness-index	=	Homing toward healthy	+	Volatility of random noise

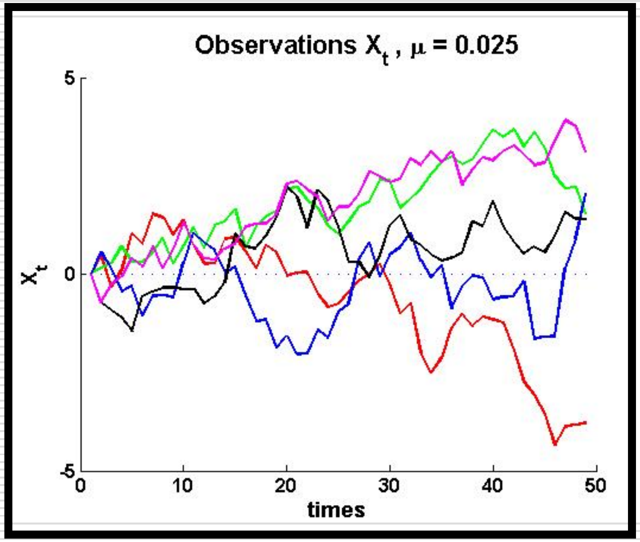
- Note that depressive and manic states were quantified by psychiatrists using the popular Hamilton and Young scores

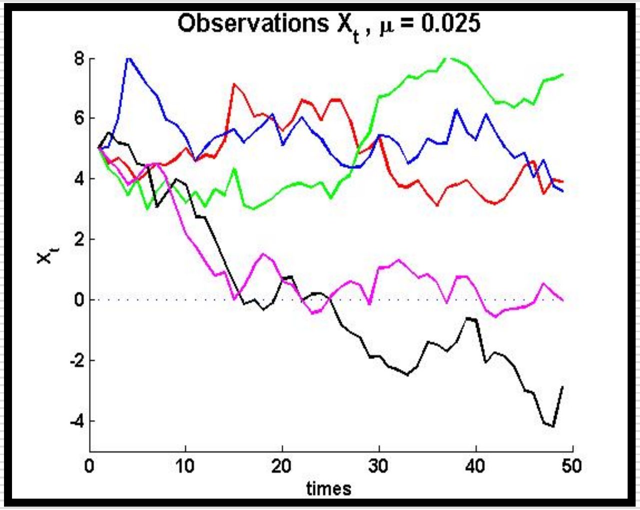
Model Behavior Effect of μ - homing toward normal



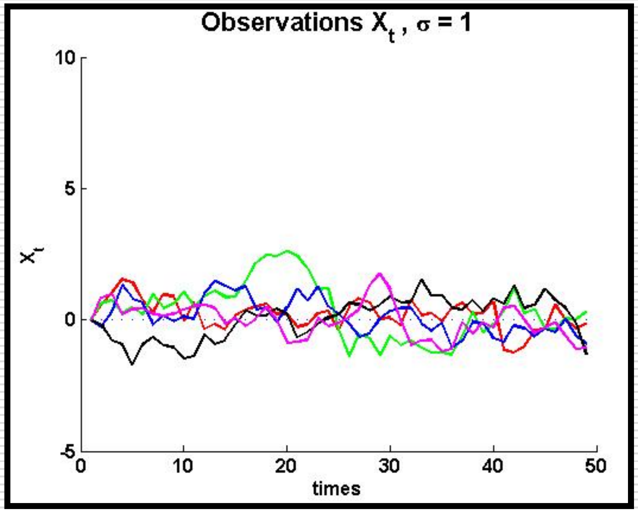
$\sigma = 1$



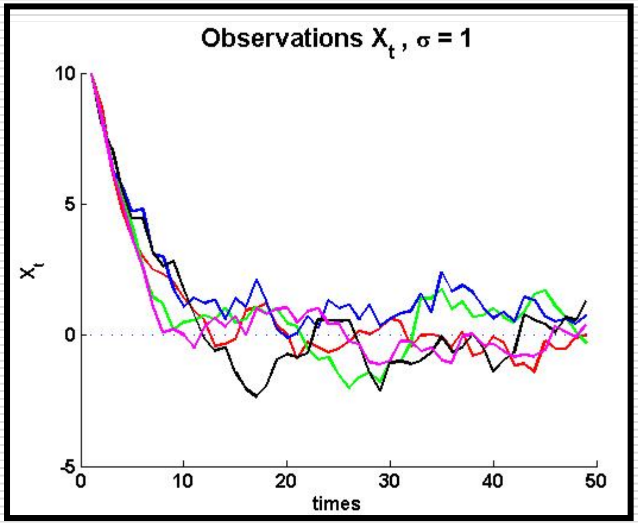


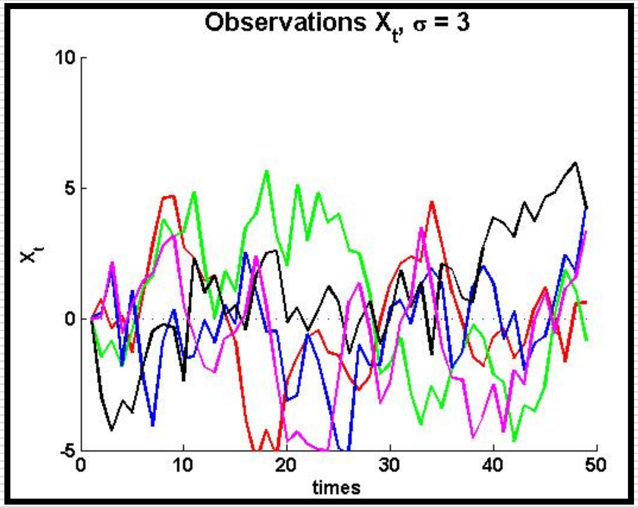


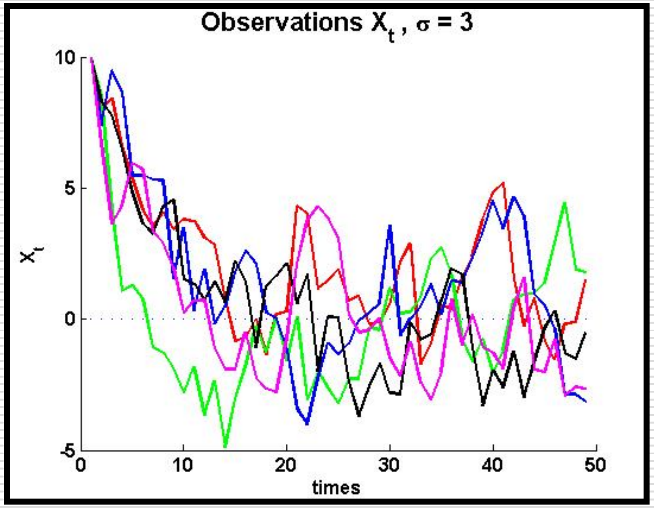
Model Behavior Effect of σ - volatility



$\mu = 1$



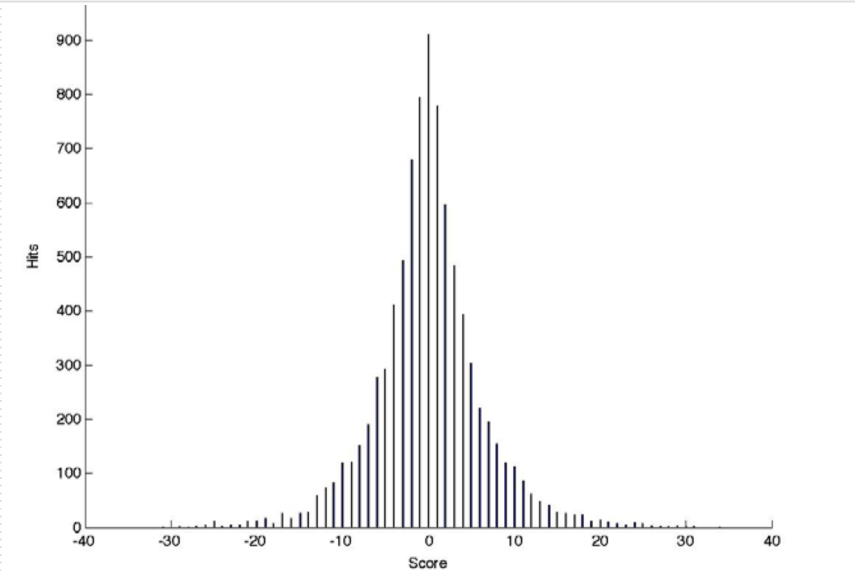




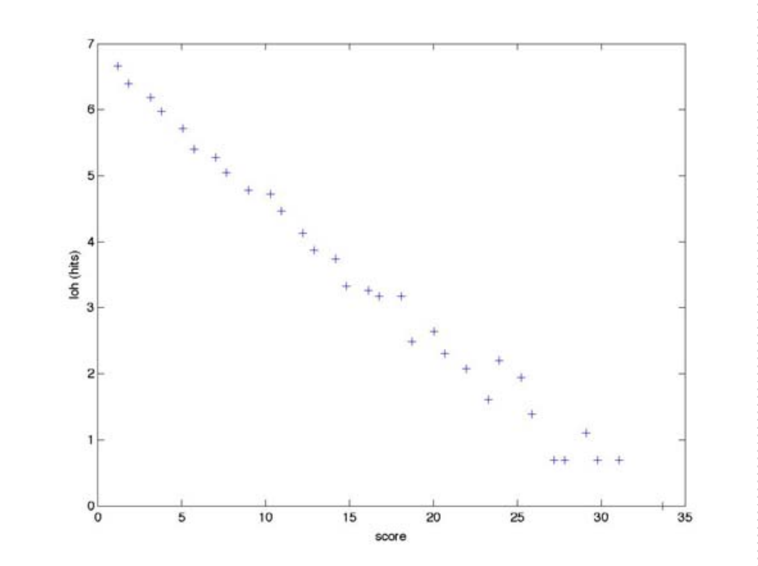
Noise characterization

- Quantitative - analyze distribution of points
- Qualitative - consider how the moods of bipolar patients change
- Determine whether real and simulated charts can be distinguished

Steeple-shaped histogram



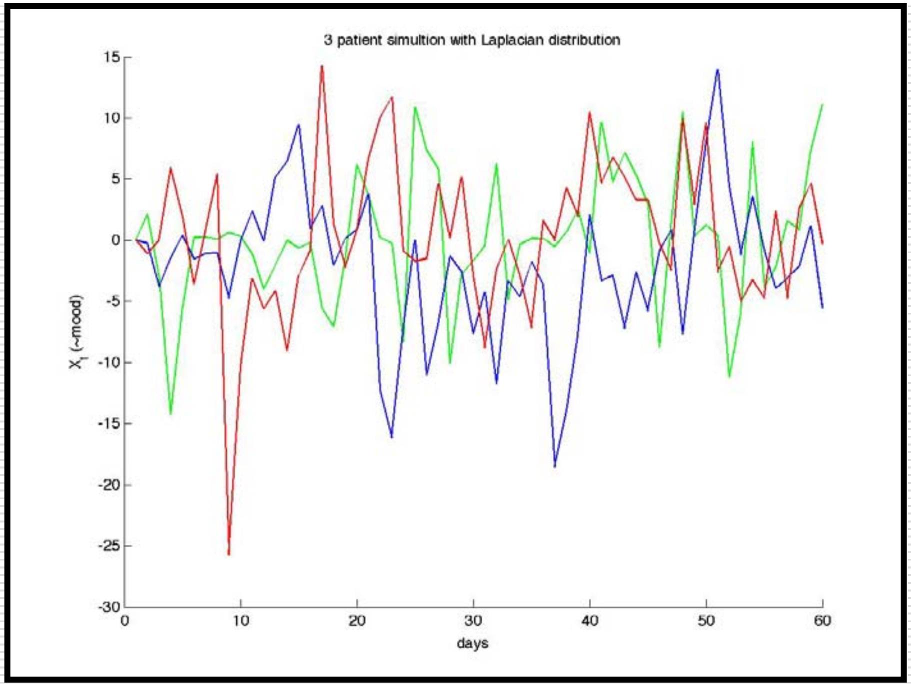
Double exponential



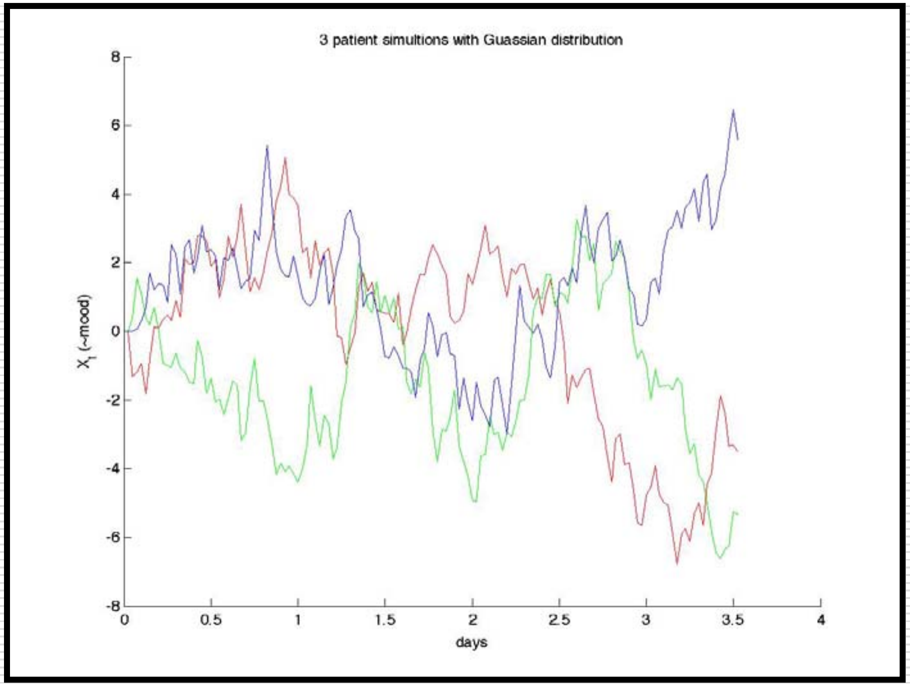
Noise with a Laplacian distribution

A noisy comparison

- Laplace



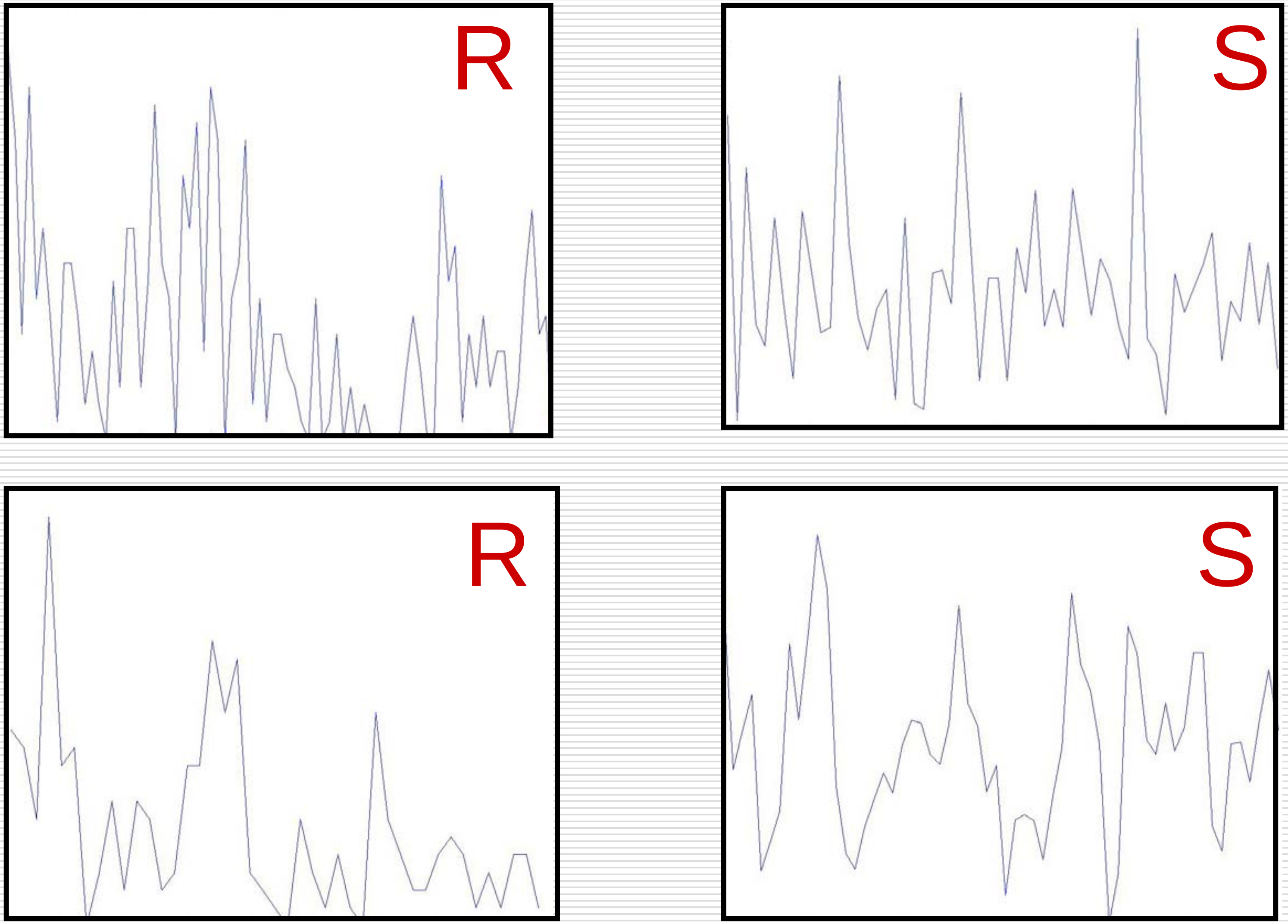
- Gaussian



Note more severe change

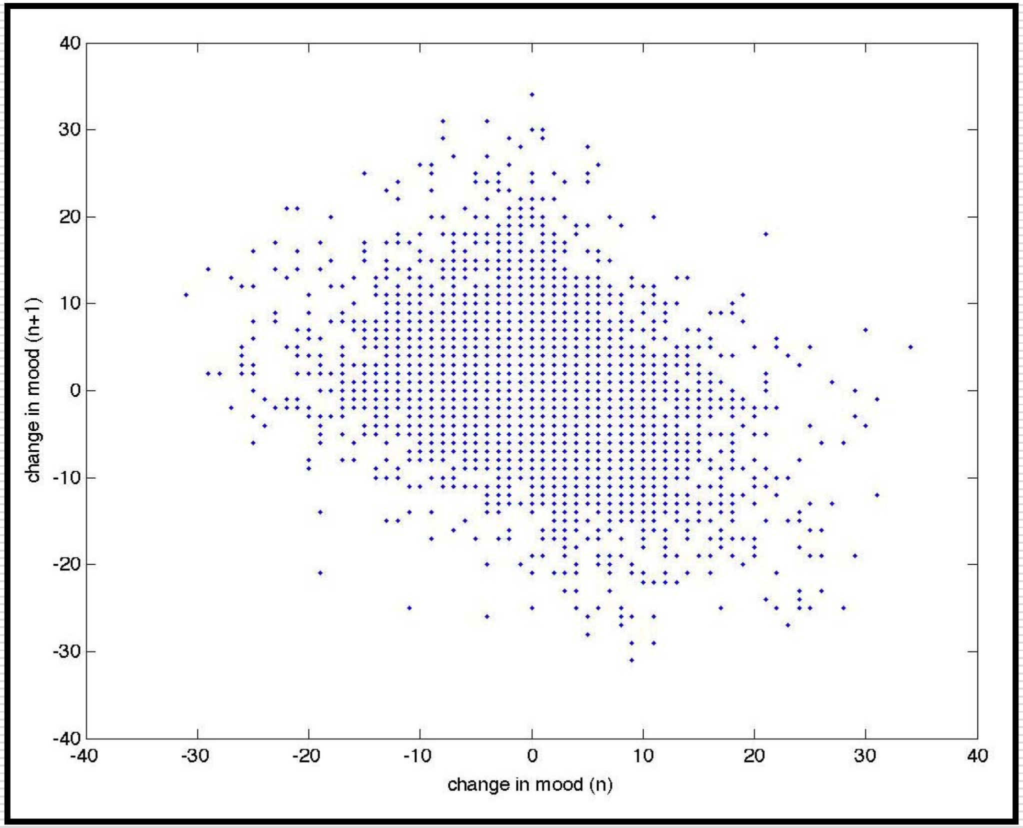
Note more gradual change

Can you tell real from simulated?



A Markov Model

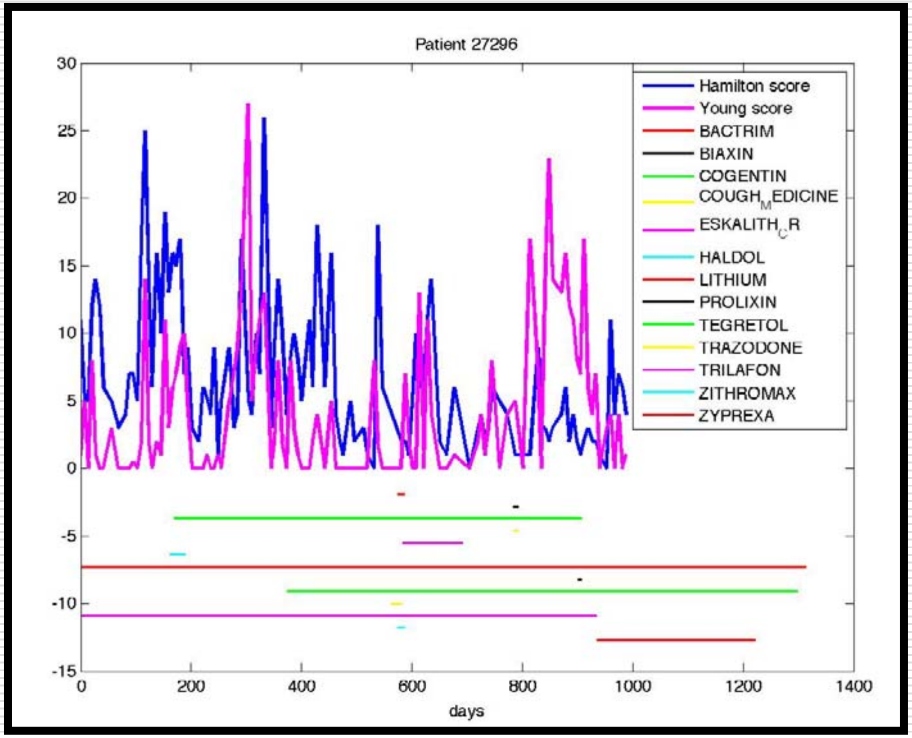
- Without memory
  - Change in mood depends only on its state today and not on previous days



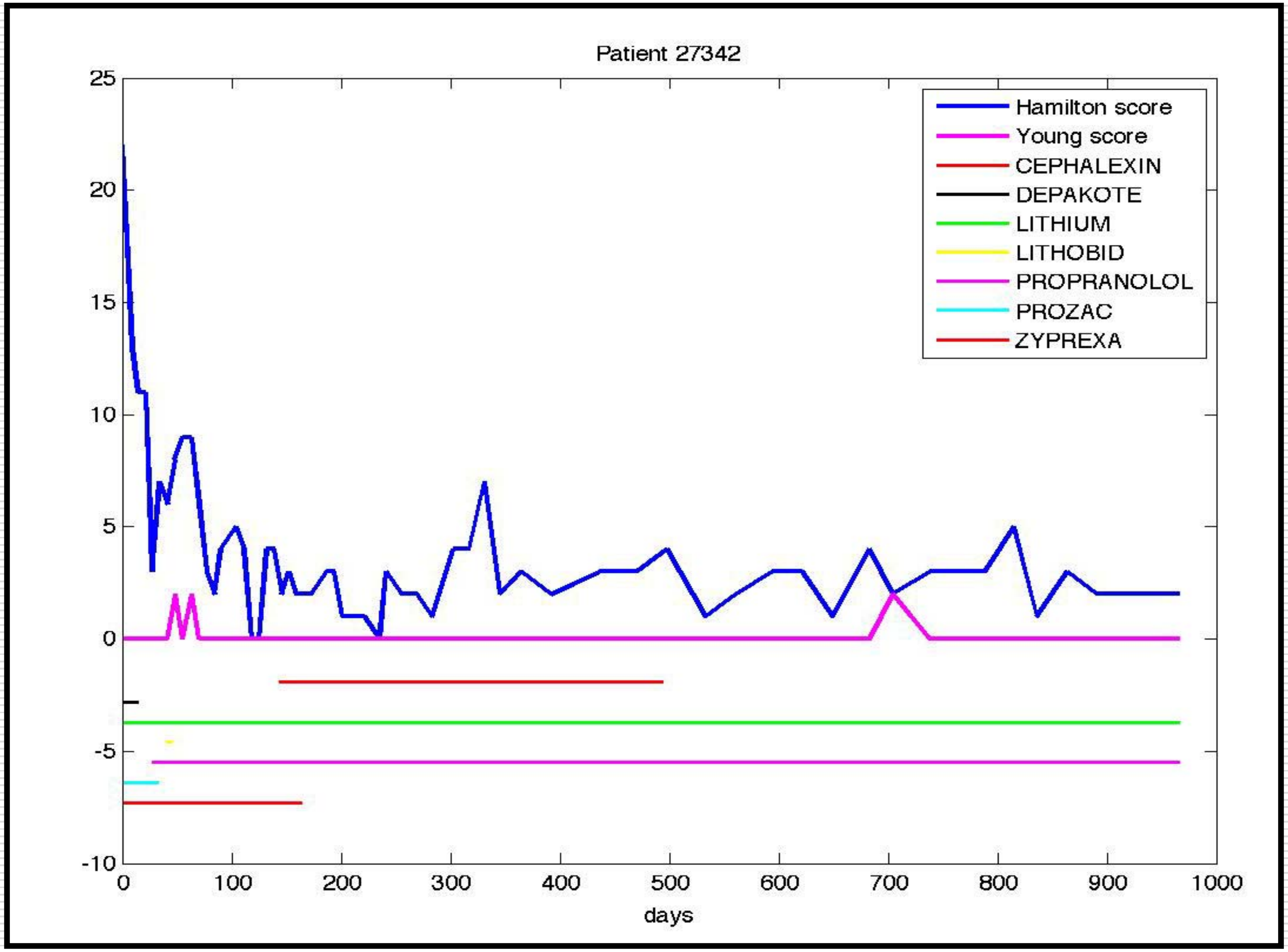
Evaluating the benefit of treatment

- Difficult to approach
  - Multiple medications
  - Delay of effect
  - Short treatment times
  - Effect of counseling and environment
- Compare patterns before and after treatment
  - Noise
  - Parameter values
    - Extremes - σ
    - Cycling - μ

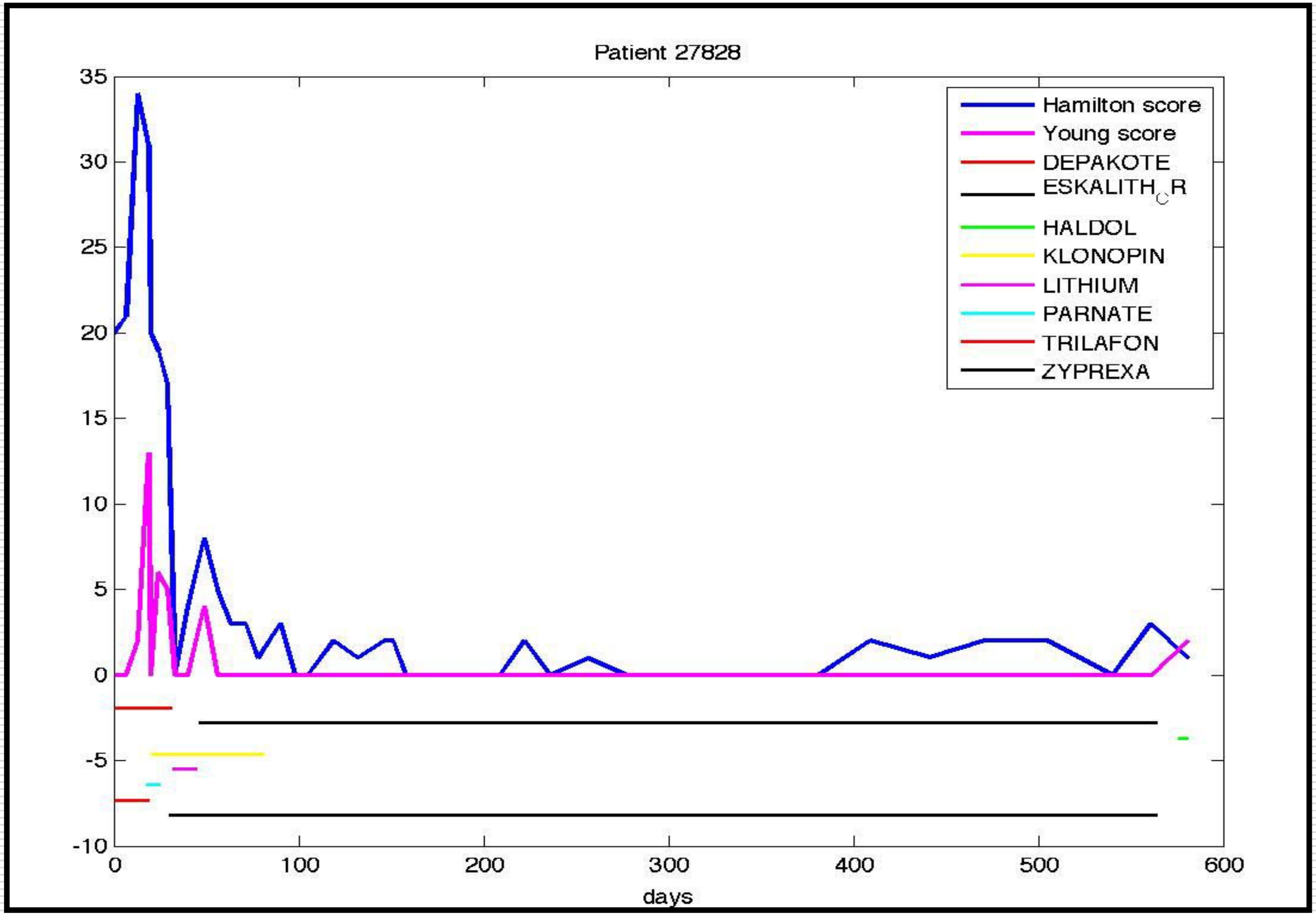
<u>A troubled patient: 13 meds</u>



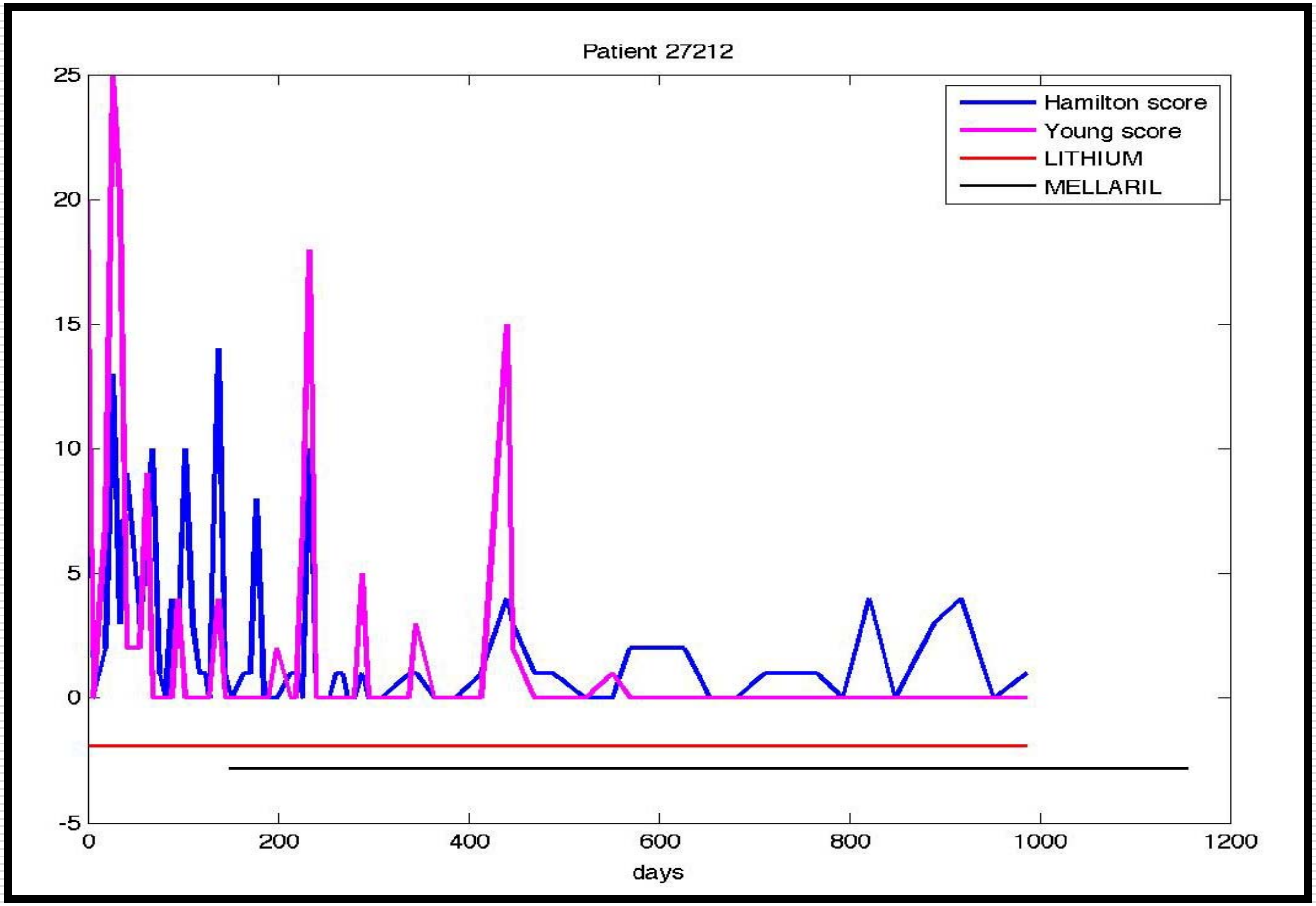
Patients who improve with treatment



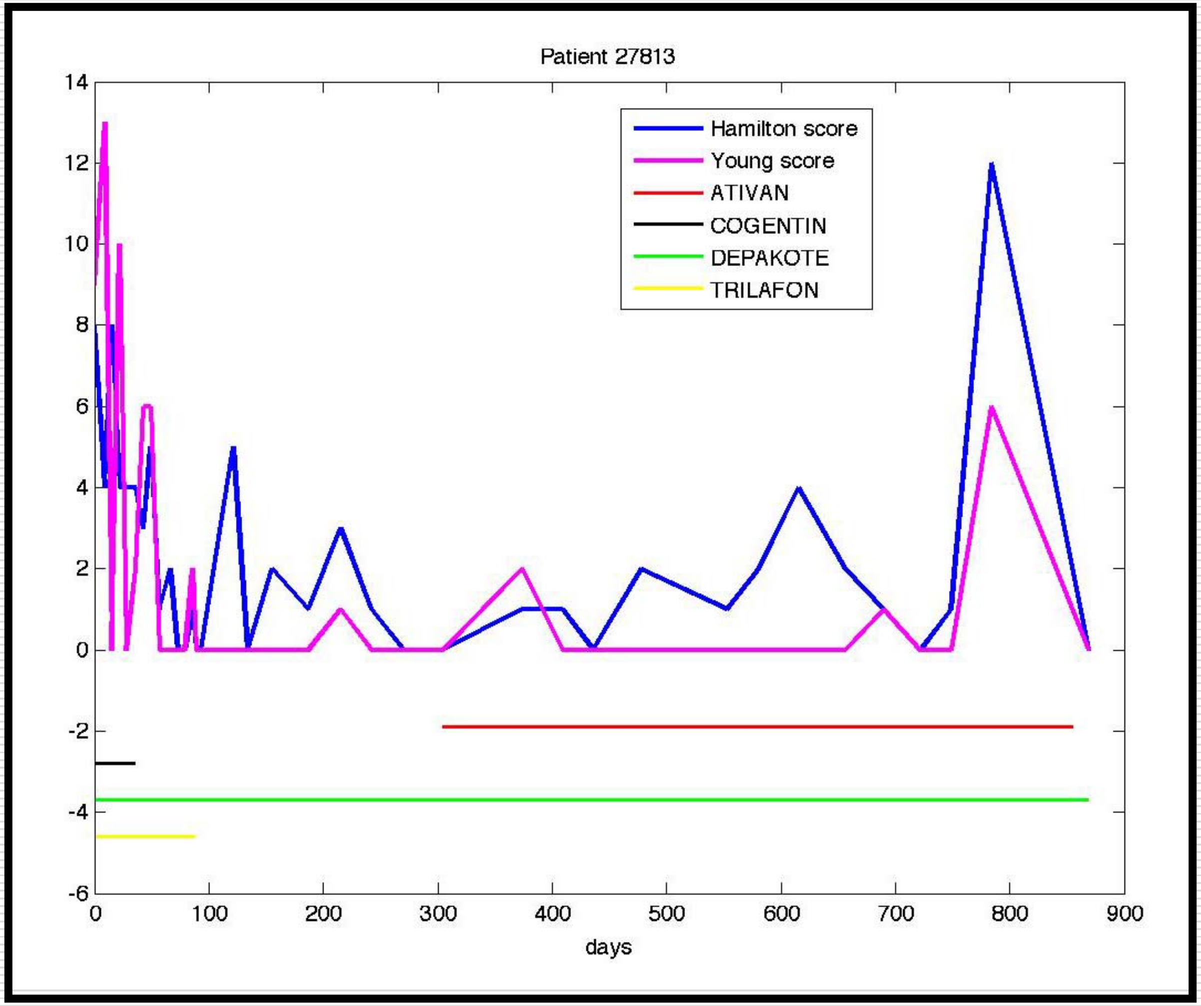
Patients who improve with treatment



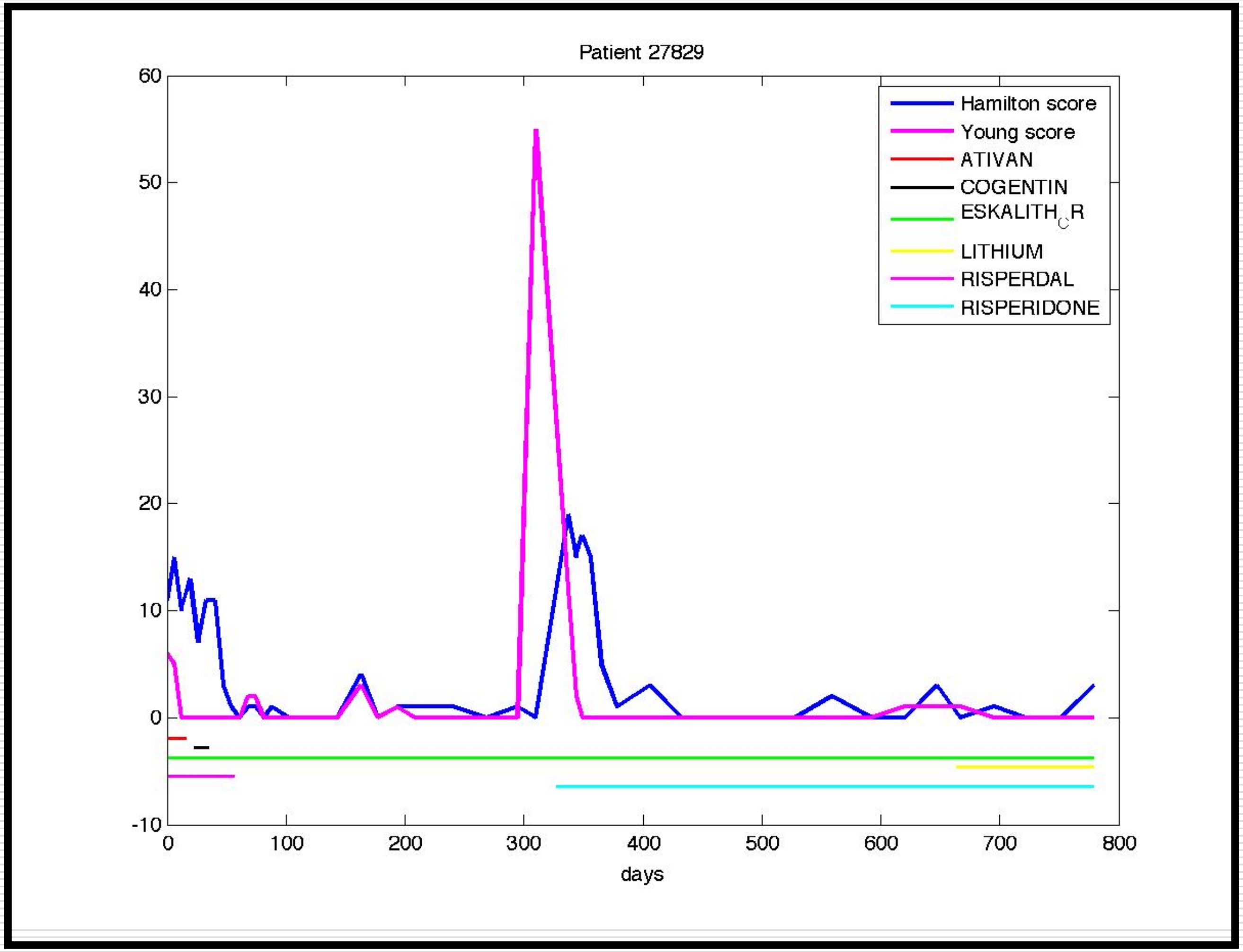
Patients who improve with treatment



Patients in remission who have an episode



Patients in remission who have an episode



Pattern recognition and grouping are key

- Hypothetical patterns
  - Sigma decreases after start of treatment
    - Medicine is helping
  - A patient has a small homing value
    - Lithium, a mood stabilizer, will be most helpful
  - Noise changes from Laplacian to Gaussian distribution after start of psychotherapy
    - Patient is in remission

Conclusions

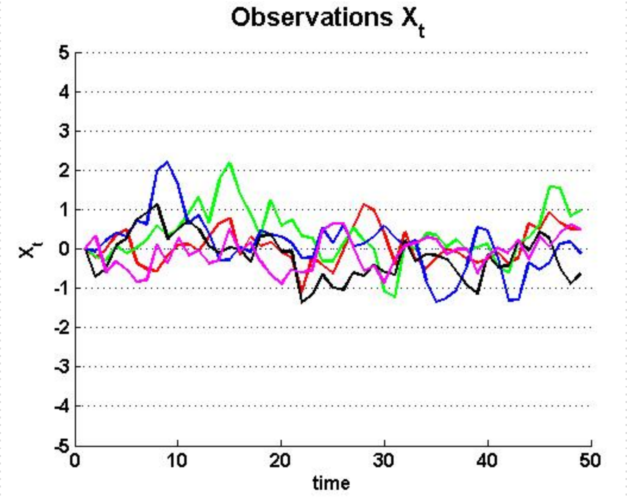
- A stochastic model with two patient-dependent parameters is sufficient to model patient mood.
- The moods of bipolar patients have a Laplacian distribution.
- This is a Markov model.

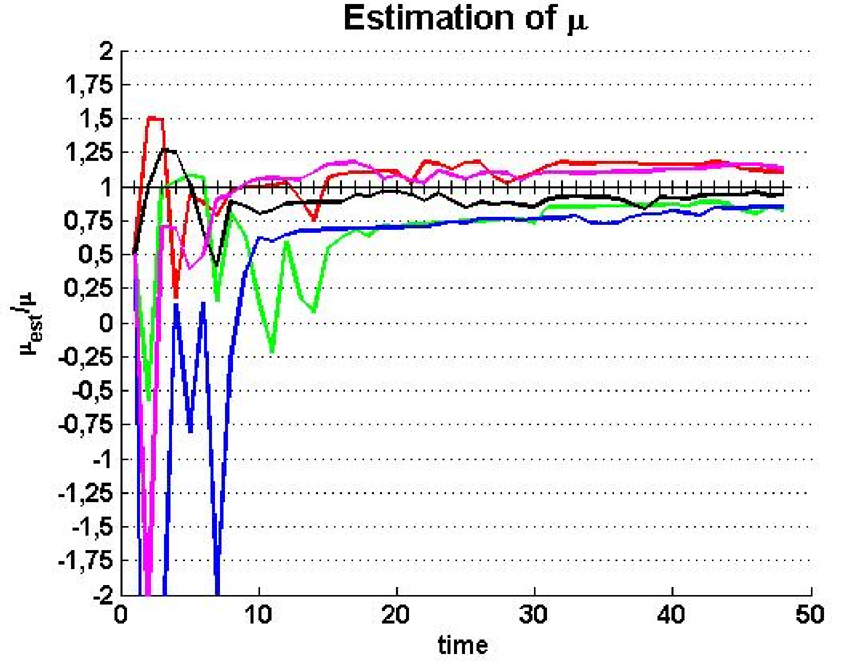
Future Work

- Analyze patterns before and after treatments
- Develop groups
- Parameter estimation

Outlook Parameter estimation

Five simulated patients





About 14 data points are needed for a reasonable estimation of σ, μ

Acknowledgements

BBSI @ Pitt 2006

Shlomo Ta'asan

Eva Eggeling

References

1. NIH Publication No. 01-4595 (2001). "Going to Extremes: Bipolar Disorder."
2. World Health Organization. A54/DIV/4 (2001). "Ministerial Round Tables: Mental Health."
3. Goodwin, FK and Jamison KR. *Manic-depressive Illness.* New York: Oxford University Press, 1990.
4. J Clin Psychiatry. 2000;61 Supp 13:38-41. "The economic burden of bipolar disease."