A Novel Dynamical Systems Approach to Statistical Mediation Analysis

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Talk Overview

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- Main goal is to describe an approach that connects statistical mediation analysis with dynamical systems modeling.
- Motivation comes from the challenges (and opportunities) presented by intensive longitudinal data.
- Some additional considerations:
  - The analysis applies in either idiographic or nomothetic settings.
  - Presentation restricted to constant coefficient models (linear time-invariant systems) for the sake of simplicity.

To download this talk...

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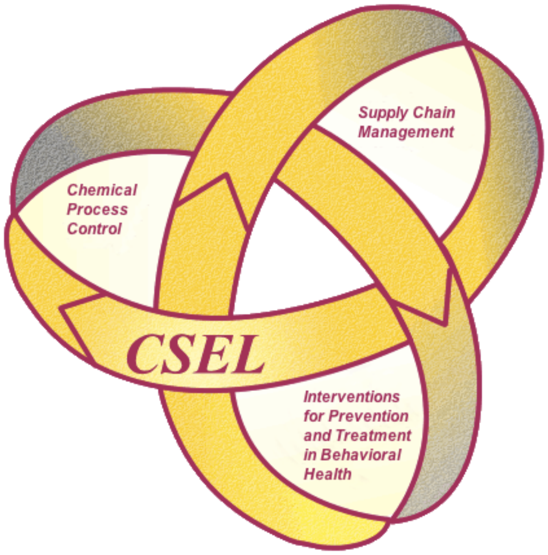

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Why dynamical systems for statistical mediation analysis?

- Serves to better understand the concepts of *change* and *effect* in interventions, this includes:
  - how often to measure
  - within and between participant variability
- Allows better use of intensive longitudinal data.
- Expands the view of moderation, confounding, and other phenomena associated with statistical mediation analysis.
- Enables the application of *control engineering principles* for accomplishing adaptive time-varying interventions.

Smoking Cessation Intervention

- Data from study described in McCarthy *et al.*, *Addiction*, Vol. 103, pgs. 1521-1533, 2008. Active drug is buproprion SR.
- 11 week study; randomization (*n = 463*)
  - Drug: Drug, Placebo
  - Counseling: Yes, No
- Treatment Conditions:
  - Active Drug with Counseling (AC; *n=101*)
  - Active Drug, No Counseling (ANc; *n = 101*)
  - Placebo with Counseling (PC; *n =100*)
  - Placebo, No Counseling (PNc ; *n =101*)
- *T = 42* daily observations for each participant

Measurements

- *Outcome*: Number of Cigarettes Smoked
- *Mediator*: Craving, determined as the sum of four scores:
  - How strong was your urge to smoke?
  - How much have cigarettes been on your mind?
  - How much have you thought about smoking?
  - How bothered were you by a desire to smoke?
- *Treatment* = 0 (pre) and = 1 (post) quit.

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Smoking Cessation Intervention AC and PNc Cohort Average Data

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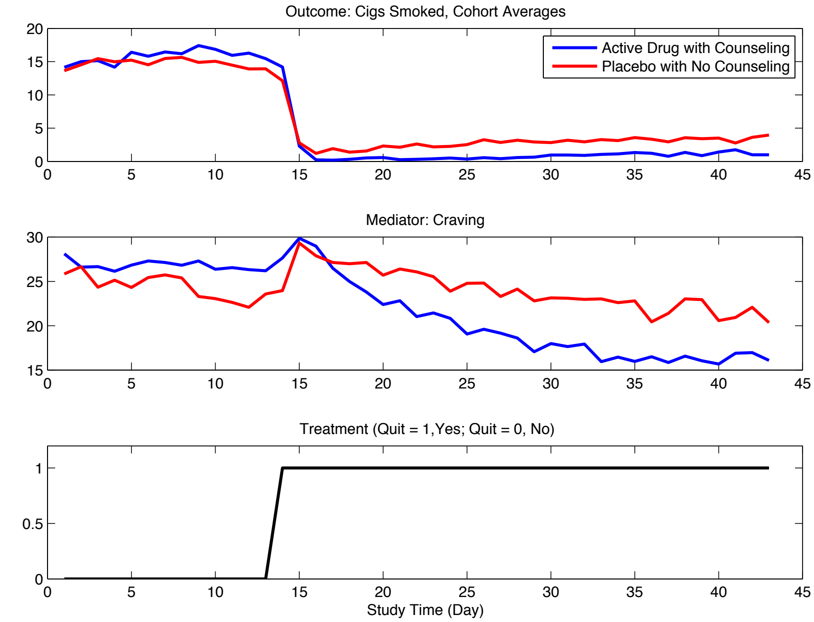

- Comparison of average cigarettes smoked and craving scores for two treatment groups (active drug with counseling (blue) vs. placebo-no counseling (red)).

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Representative Participants "A" and "B"

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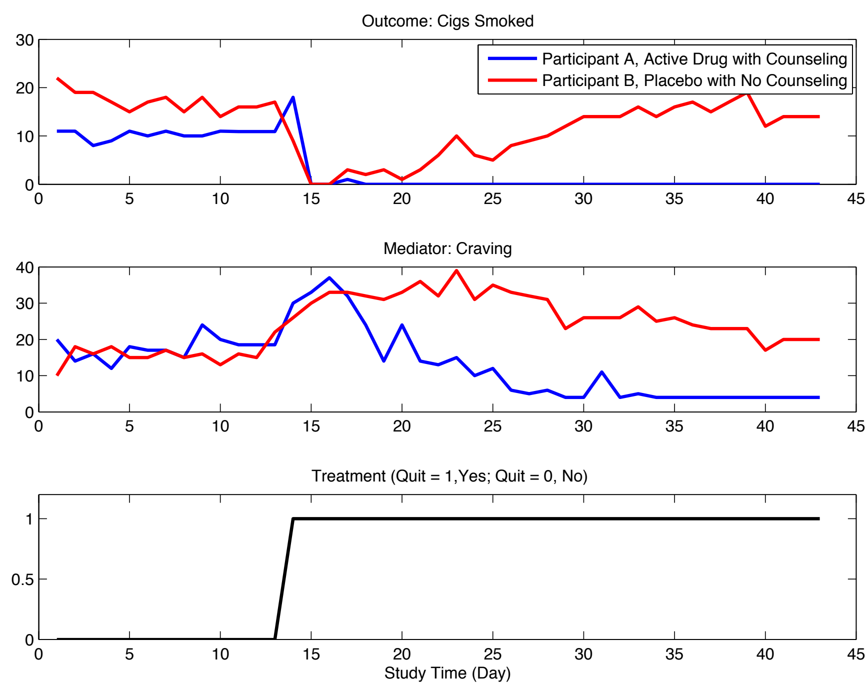
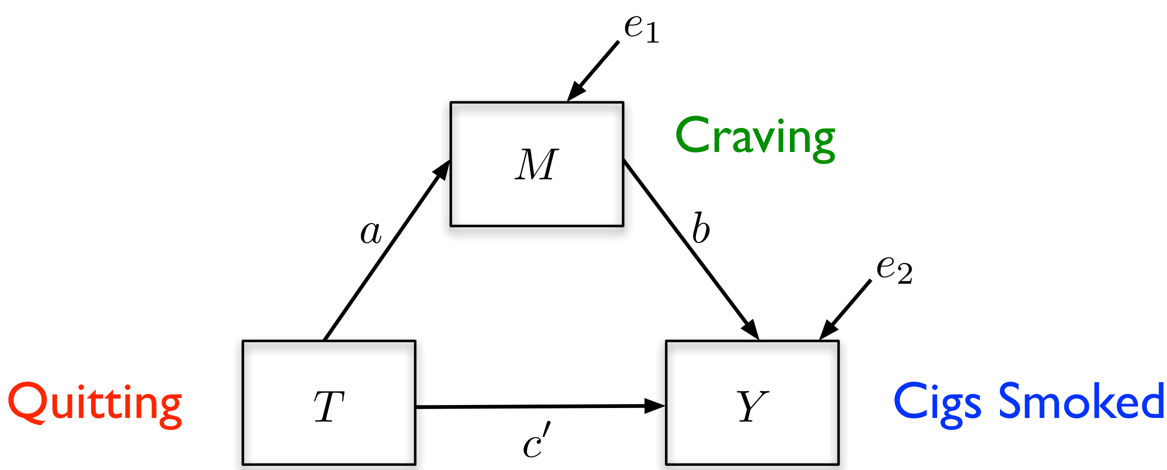


- Participant "A" from AC cohort (blue); participant "B" from PNc cohort (red)

Standard Mediation Model



$$
\begin{aligned}
Y &= \beta_{o_2} + c'T + bM + e_2 \\
M &= \beta_{o_1} + aT + e_1
\end{aligned}
$$

All variables observed; *M* and *Y* continuous; *T* can be categorical

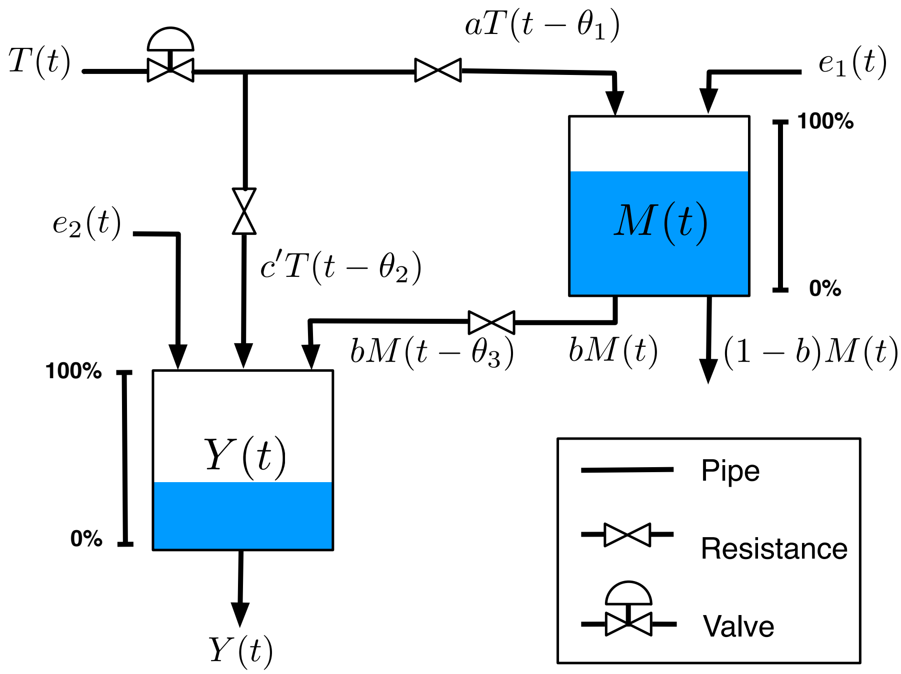
Dynamic Fluid Analogy (applies to any path diagram)

- All exogeneous observed variables are treated as external "inlet flows"
- All endogeneous observed variables are treated as "inventories"
- The principle of conservation of mass is applied:

Accumulation within the System = Inflow through the System Boundaries - Outflow through the System Boundaries

The resulting dynamical model matches the standard SEM model for the path diagram at steady-state!

Fluid Analogy (for model based on first derivatives)

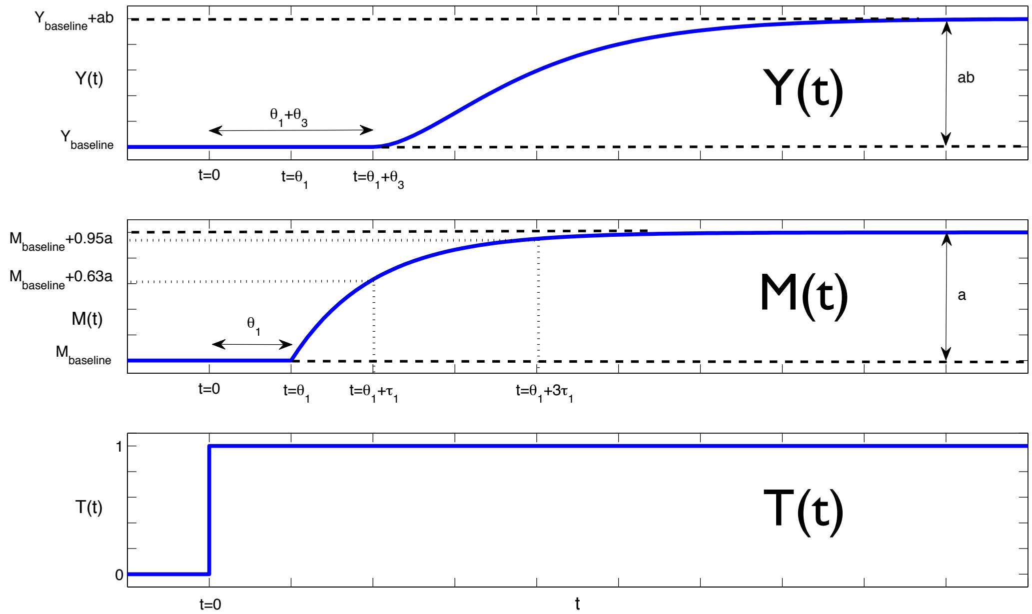


Differential Equation Model (using first-derivatives)

$$
\begin{aligned}
\tau_1 \frac{dM}{dt} &= a\,T(t-\theta_1) - M(t) + e_1(t) \\
\tau_2 \frac{dY}{dt} &= c'\,T(t-\theta_2) + b\,M(t-\theta_3) - Y(t) + e_2(t).
\end{aligned}
$$

where:
τ_1 and τ_2 are time constants,
$\theta_1, \theta_2, \theta_3$ are time delays,
a, b, c' are system gains and
$e_1(t)$ and $e_2(t)$ are disturbances.

Mediator and Outcome Response, Step Change in Treatment



$$\theta_1 = \theta_3 = 1, \tau_1 = \tau_2 = 1, a = b = 1, c' = 0, e_1 = e_2 = 0$$

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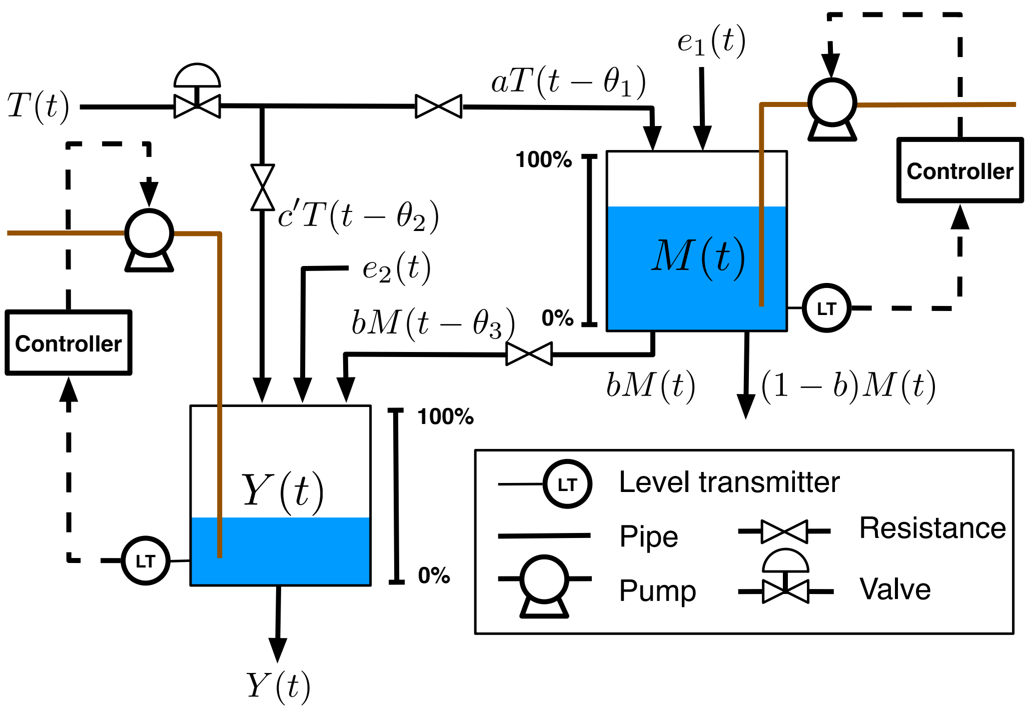
Fluid Analogy

(for model based on second derivatives)



Differential Equation Model
(using second derivatives)

$$
\begin{aligned}
\tau_1^2 \frac{d^2M}{dt^2} + 2\zeta_1\tau_1\frac{dM}{dt} &= a\left(T(t-\theta_1)+\tau_a\frac{dT(t-\theta_1)}{dt}\right) \\
&\quad -M(t)+e_1(t) \\
\tau_2^2 \frac{d^2Y}{dt^2} + 2\zeta_2\tau_2\frac{dY}{dt} &= c'\left(T(t-\theta_2)+\tau_{c'}\frac{dT(t-\theta_2)}{dt}\right) \\
&\quad +b\left(M(t-\theta_3)+\tau_b\frac{dM(t-\theta_3)}{dt}\right) \\
&\quad -Y(t)+e_2(t).
\end{aligned}
$$

where:
τ_1 and τ_2 represent the natural time period,
ζ_1, ζ_2 are damping coefficients and
$\tau_a, \tau_b, \tau c'$ are related to the system zeros.

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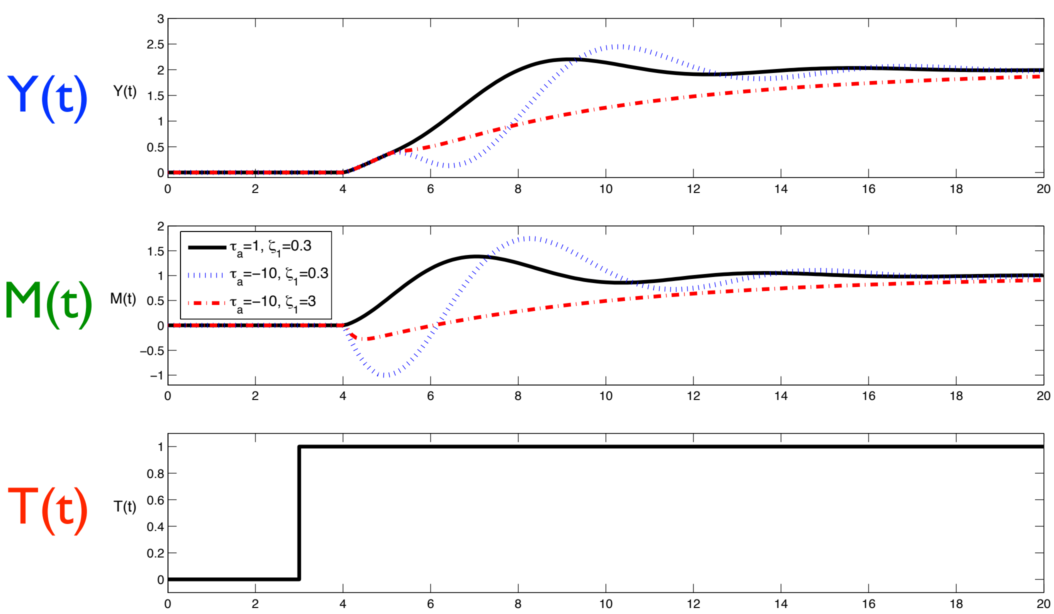
Second-Order Responses
(illustrative examples)

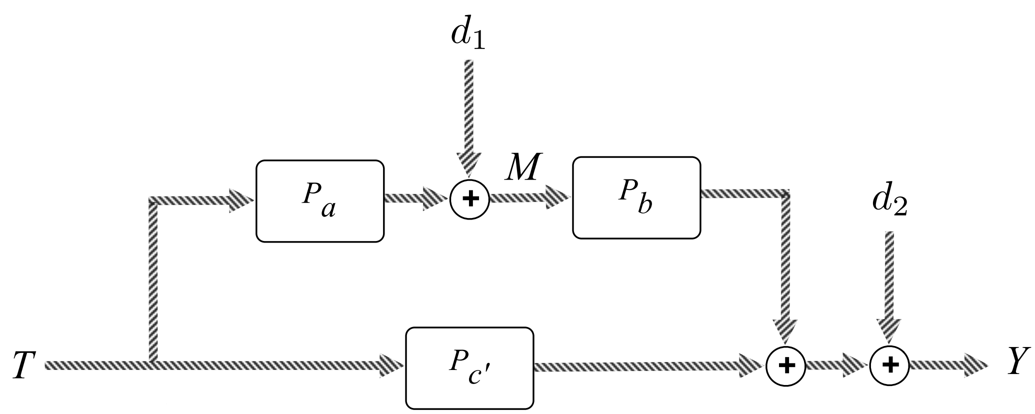


$$\theta_1 = \theta_2 = \theta_3 = 1, \tau_1 = \tau_2 = 1, a = b = c' = 1, e_1 = e_2 = 0$$
$$\tau_b = \tau_c = 1, \zeta_2 = 1$$

Implications, Observations

- Steve Boker (U.Va.) and Matt Fritz (VPU) have done work that overlaps with our analysis; however, our approach, interpretation, and presentation are novel and distinctive.
- *Functional data analysis* (FDA) is well-suited as a parameter estimation scheme for this model; estimating time-varying coefficients is a natural extension of this work (Trail *et al.*)
- The proper choice of *sampling interval* is a very important consideration in this type of analysis.
- *Model parsimony* is an appealing aspect of differential equation modeling, given the diversity number of response types that can be obtained from a relatively small number of parameters.

Transfer Function Representation for Mediation Analysis



- A *signals and systems* block diagram, not a path diagram.
- *Pa*, *Pb*, and *Pc'* represent *transfer functions*; these are compact representations of differential equation models
- Arrangement allows for a generalization of dynamic mediation analysis beyond fluid analogies.

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Parameter Estimation Summary

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$$\tau_1\tau_2\,\frac{d^2M}{dt^2} + (\tau_1+\tau_2)\,\frac{dM}{dt} + M(t) \;=\; a\,(T(t) + \tau_a\frac{dT}{dt})$$
$$\tau_3\;\tau_4\,\frac{d^2Y}{dt^2} + (\tau_3+\tau_4)\,\frac{dY}{dt} + Y(t) \;=\; c'\,(T(t) + \tau_3\frac{dT}{dt}) + b\,(M(t) + \tau_4\frac{dM}{dt})$$

Data Set	*Cohort Average, Active Drug with Counseling*	*Cohort Average, Placebo with No Counseling*	*Participant A, Active Drug with Counseling*	*Participant B, Placebo with No Counseling*
Mediator Fit [%]	86.12	63.74	65.70	47.70
Outcome Fit [%]	84.85	88.05	74.02	58.88
a	-11.088	-3.779	-18.539	2.611
τ_1	7.669	17.090	6.009	1.722
τ_2	0.281	0.001	0.001	13.424
τ_a	-3.275	-28.014	-7.314	107.125
c'	-15.873	-10.979	-11.880	6.119
τ_4	0.507	0.001	0.188	9.511
b	-0.087	-0.286	0.004	-0.762
τ_3	0.782	0.977	0.001	0.006

- Parameter estimation performed using the **Process Models** feature in Matlab's System Identification Toolbox (one-step ahead prediction-error minimization for continuous differential equation structures).

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Dynamical Model Fits for Cohort Averages

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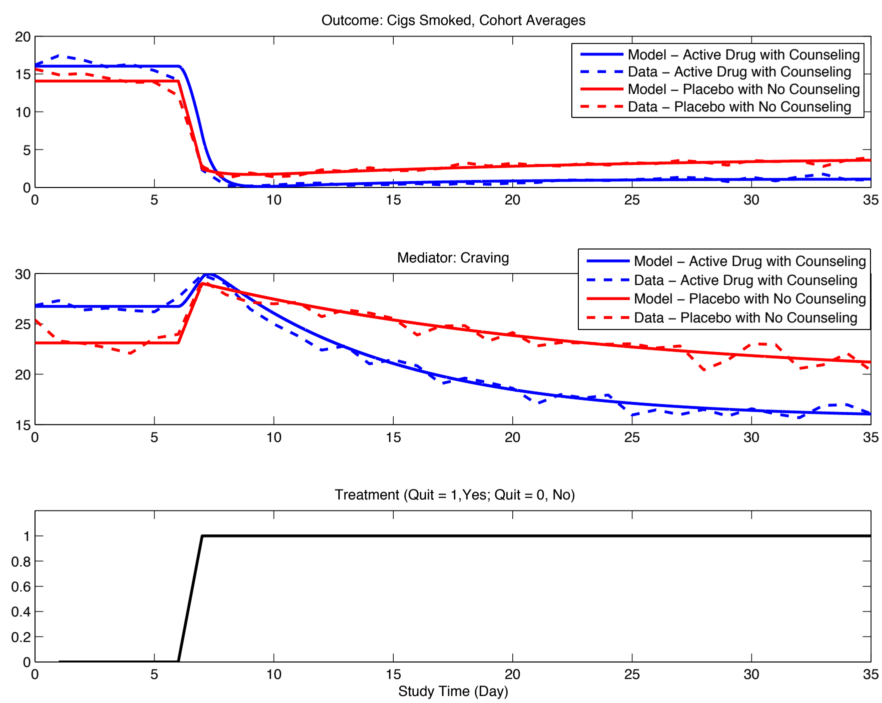

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Dynamical Model Fits for Participants "A" and "B":

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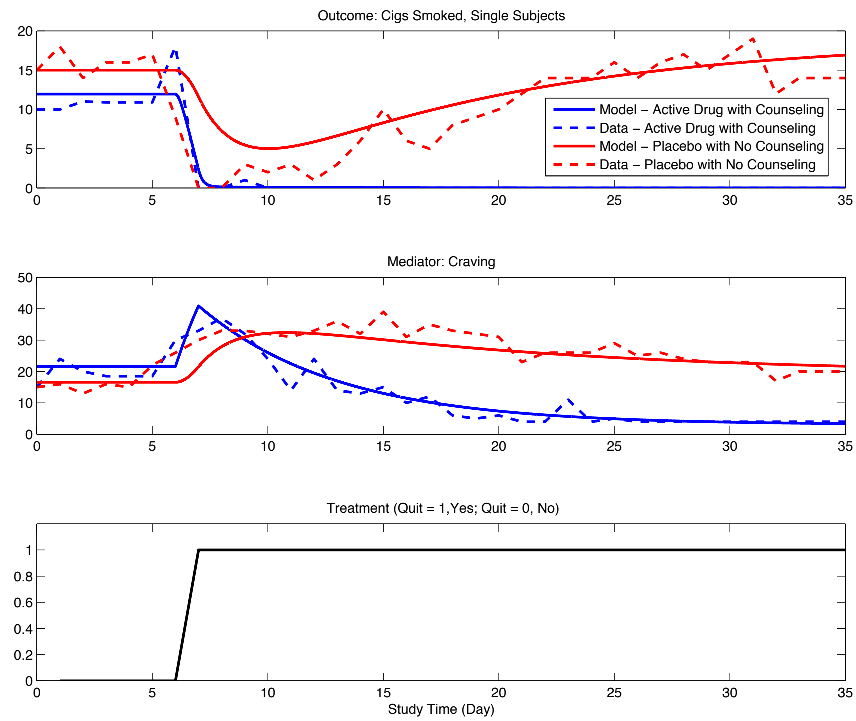

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Summary and Conclusions

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- A novel dynamical systems approach to statistical mediation analysis has been presented.
- The method stems from a *fluid analogy* of the mediation process, in which mediator and outcome variables are treated as inventories, and treatment corresponds to an inflow. The approach can be extended to any path diagram.
- A generalization based on *transfer functions* was presented.
- The resulting differential equations can be estimated from data using algorithms from system identification.
- The method was shown as successful in describing the dynamics of data (both cohort averages and individual participants) in a smoking cessation study conducted by UW-CTRI.

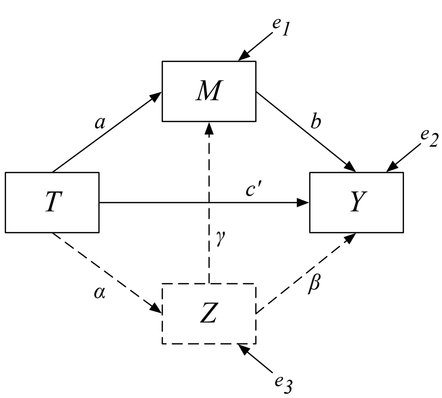
Some Questions and Issues to Consider

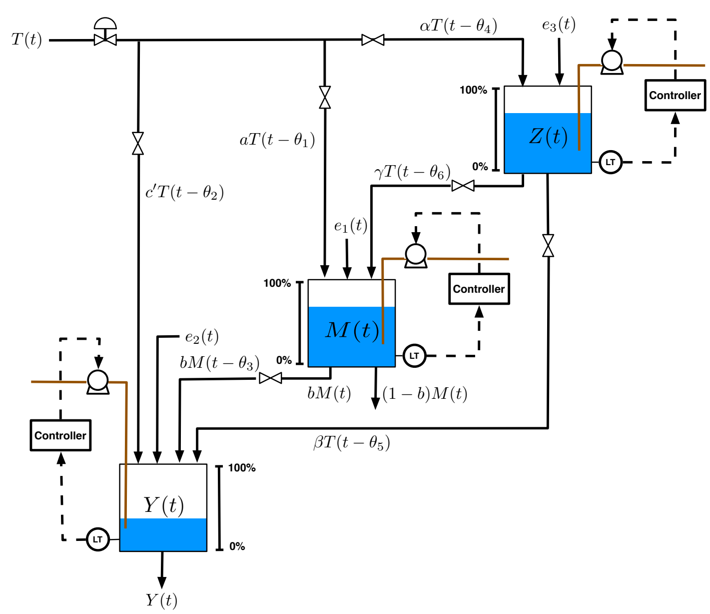
- How can *behavioral theories* be reconciled with the physical (fluid) analogies that have been presented?

- *Experimental design* in support of dynamic mediation modeling represents an interesting topic for research.

- Working towards generalized "structure-free" approaches for dynamical systems modeling of behavioral interventions that incorporate mediation, moderation, confounding, and latent variables.

Mediation with Confounding (one arrangement)





- Confounder as an additional inventory.

Acknowledgements

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- K25DA021173, "Control engineering approaches to adaptive interventions for fighting drug abuse," Mentors: L.M. Collins (Penn State) and S.A. Murphy (Michigan).

Thank you for your attention!

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