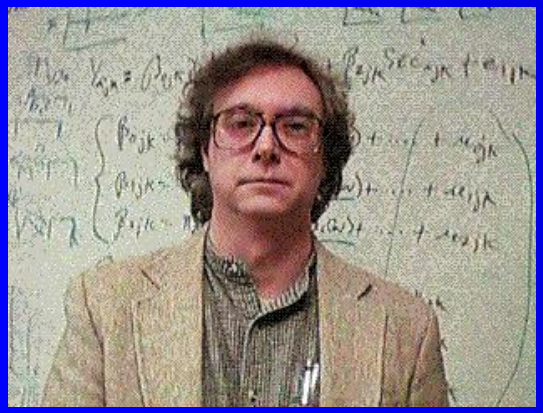
Using Dynamic Multidimensional Graphics for Obtaining Information on Hierarchical Simultaneous Time-series Measures in Infants:

Exploring Pre-modeling Conditions

The Authors



Roger L. Brown, Ph.D.

Professor and Director

Research Design & Statistics Unit, School of Nursing and Department of Family Medicine

University of Wisconsin

Suzanne Thoyre, PhD,RN

Assistant Professor and MSN Coordinator,

Neonatal Nurse Practitioner

The University of North Carolina at Chapel Hill

Karen Pridham, Ph.D., RN

Emeritus Professor

School of Nursing

University of Wisconsin

“It is important to understand what you CAN DO before you learn to measure how WELL you seem to have DONE it.”

John Tukey, 1977, Exploratory Data Analysis

Our Research Interests

What happens to various physiological measures in infants once a specific behavior(s) originated from the mother is ceased or initiated?

Some Specific Research Questions

Are there significant changes in an infants physiological response to the occurrence or lack of occurrence of a specific behavior provided by the infants mother?

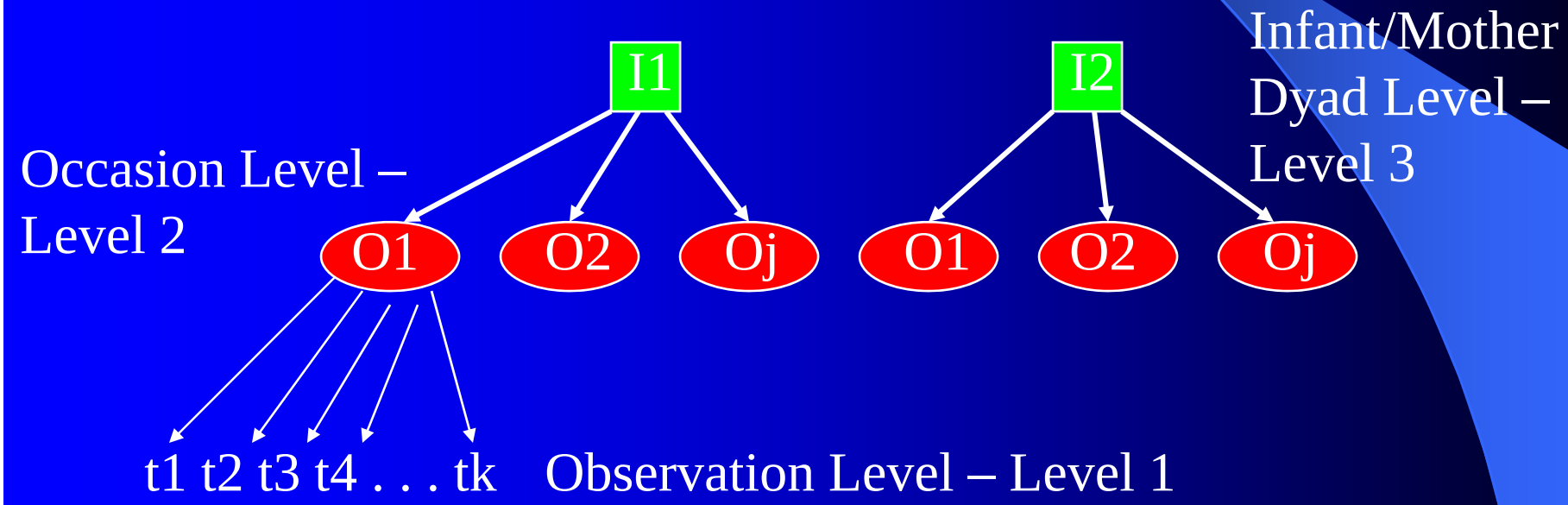
If changes are indicated, do they vary relative to certain characteristics of the infants and/or mothers?

If changes are indicated, what type of change is occurring, immediate or delayed, and what is the rate of change? Does rate of change vary and under what mechanisms?

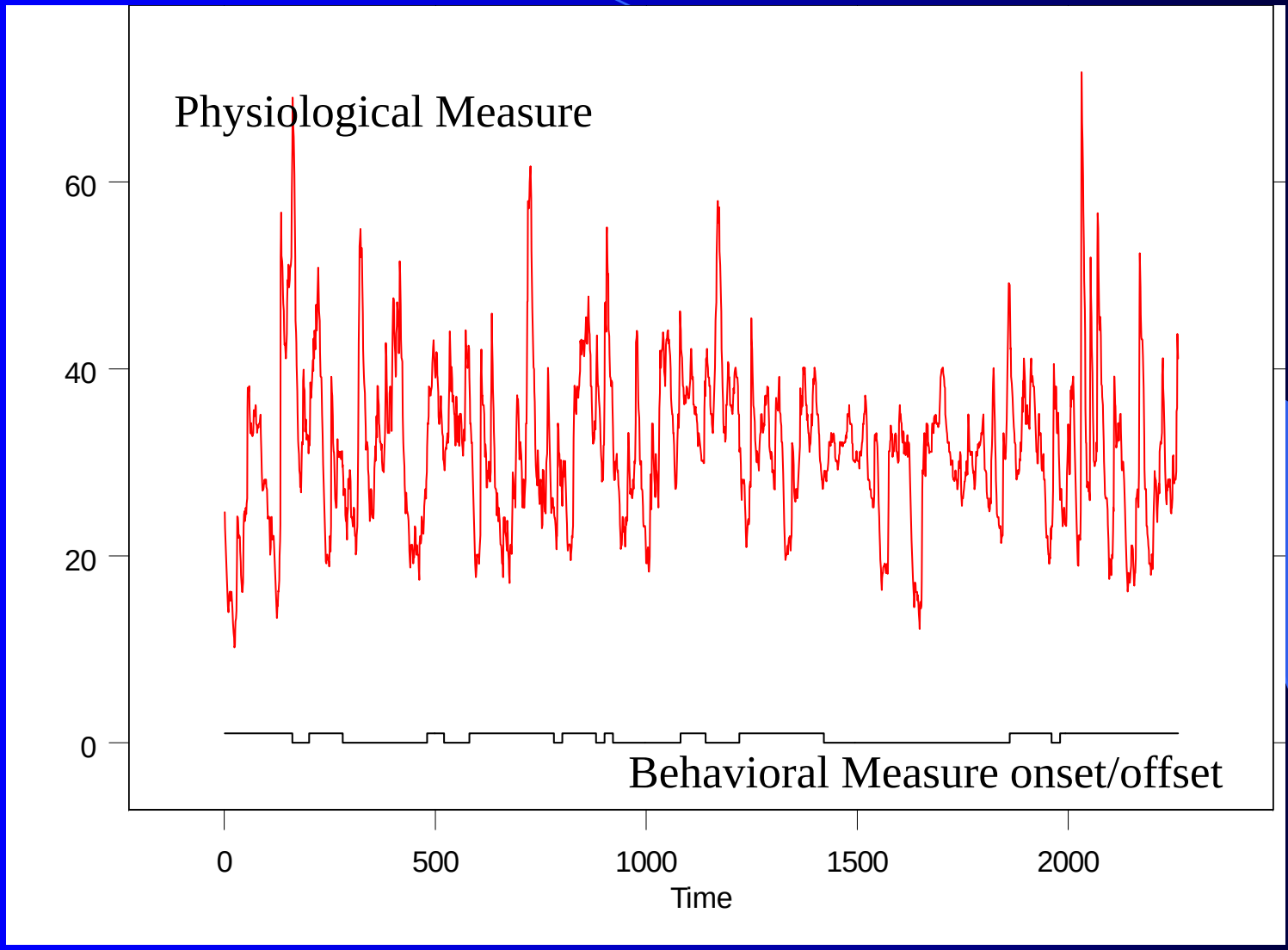
Our Analytic Modeling Strategy

Our *a priori* analytic strategy is one of modeling heterogeneity of change in infant physiology, with incorporation of theoretical explanations of differential change parameters.

Using Multilevel Modeling Techniques we have the following structure to our data

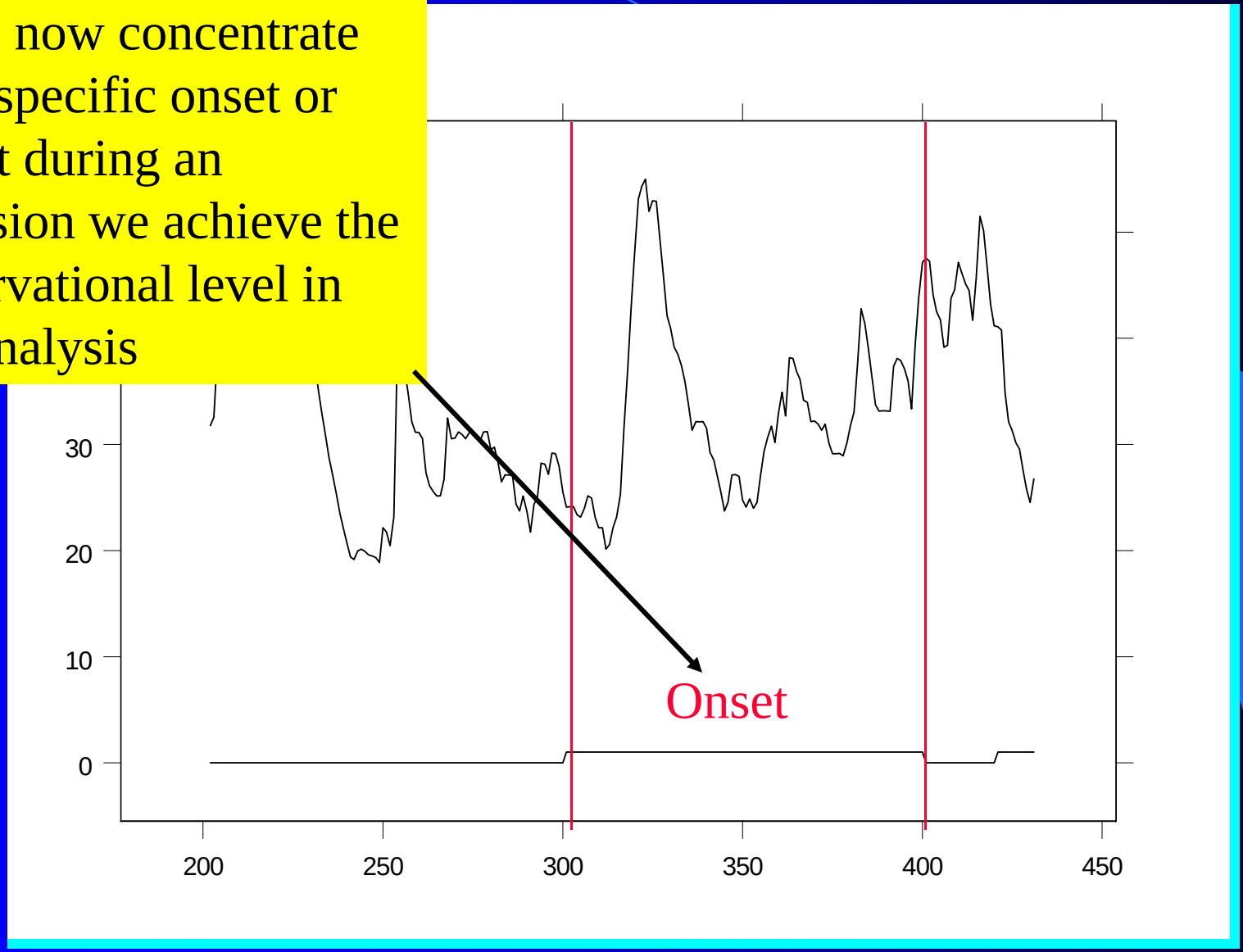


Single Occasion for an Infant/Mother Dyad



Single Observational Level Time Series

If we now concentrate on a specific onset or offset during an occasion we achieve the observational level in the analysis



Model Formulation

Assumption. We assume that Y_{tij} is the observed status at time (t) at occasion (i) for infant (j), and is a function of a systematic growth trajectory in infant physiology plus random error.

Growth in physiology is expressed in terms of a random coefficient model described as a three-level model (Goldstein, Healy, and Rasbash, 1994).

Our Analytic Modeling Strategy
Observation Level Model
Level-1

$$Y_{tij} = \pi_{oij} + \pi_{1ij}a_{1tij} + \pi_{2ij}a^{2}_{2ti} + \ldots + \pi_{pij}a^{k}_{ptij} + e_{tij}$$

Where:

Y_{tij} is a specific physiological measurement of observation (t) for occasion (i) for infant/mother dyad (j).

π_{oij} is the initial level of the physiologic measure for occasion (i) nested under infant/mother dyad (j)

a_{tij} is the number of seconds elapsed at time (t) for each occasion (i) for each infant/mother dyad (j)

π_{pij} is the growth trajectory parameter (p) for occasion (i) for infant/mother dyad (j) associated with the polynomial of degree (P).

Occasion Level Model Level-2

$$\pi_{pij} = \beta_{poj} + \sum_{q=1}^{Qp} \beta_{pqj} X_{qij} + r_{pij}$$

Where:

β_{poj} is the average initial level of the physiological measurement for each infant/mother dyad (j) in modeling the occasion initial level effect π_{oij};

X_{qij} is an occasion characteristic used as a predictor of the occasion trajectory effect π_{pij};

β_{pqj} is the corresponding coefficient that represents the direction and strength of association between occasion characteristic X_{qij} and π_{pij}; and

r_{pij} is a Level-2 random effect that represents the deviation of occasion ij's Level-1 coefficient, π_{pij}, from its predicted value based on the occasion-level model.

Infant/Mother Dyad Level Model
Level-3

$$\beta_{pqj} = \gamma_{pqo} + \sum_{s=1}^{Spq} \gamma_{pqs} W_{sj} + u_{pqj}$$

Where:

γ_{pqo} is the overall average initial level of the physiological measurement for all infant/mother dyad-level model for β_{poj};

W_{sj} infant/mother dyad characteristics used as a predictor for both level and rates of growth trajectories;

γ_{pqs} are the corresponding Level-3 coefficients that represent the direction and strength of association between infant/mother dyad characteristics W_{sj} and β_{pqj}; and

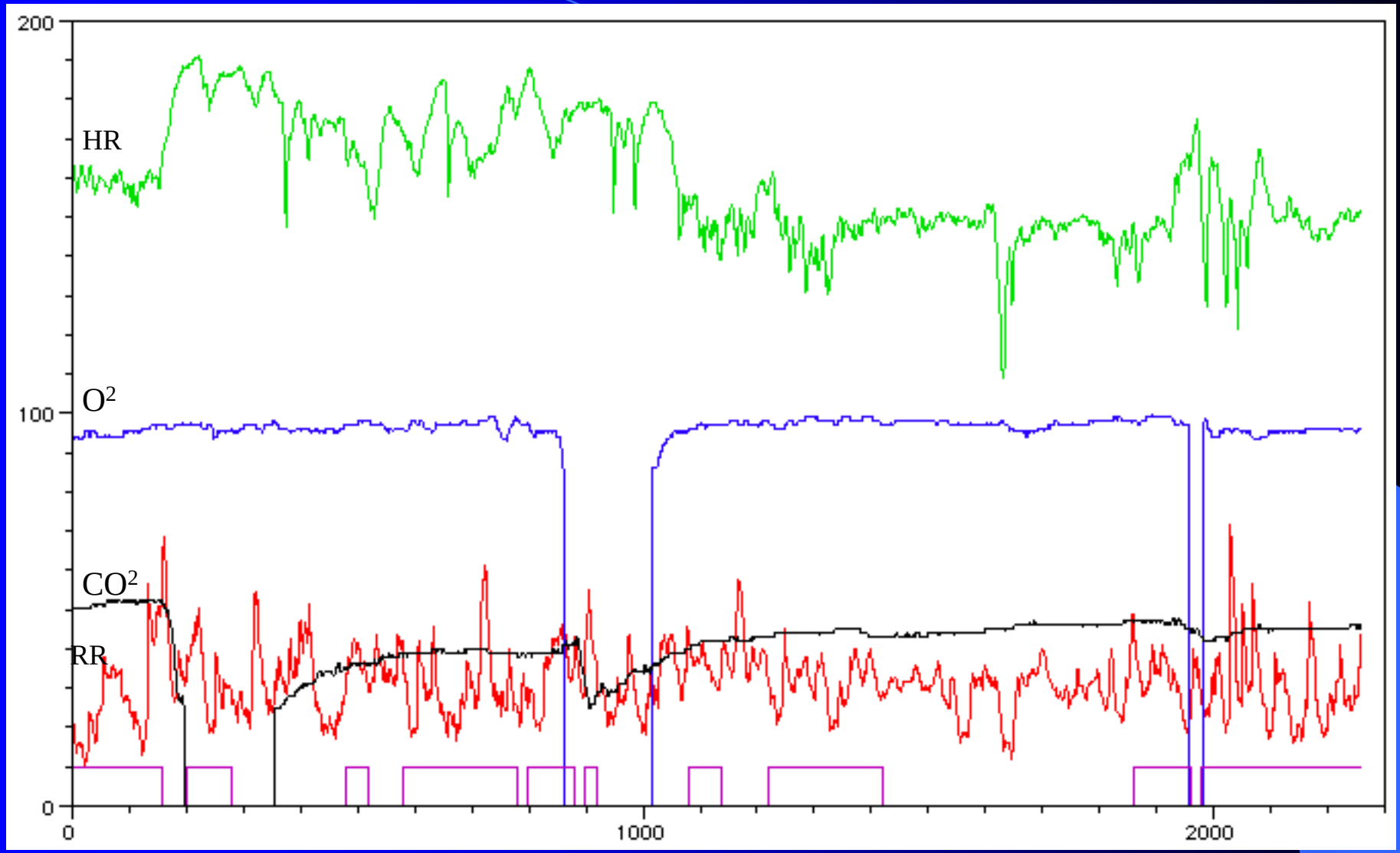
u_{pqj} is the Level-3 random effect

Methodological Problem

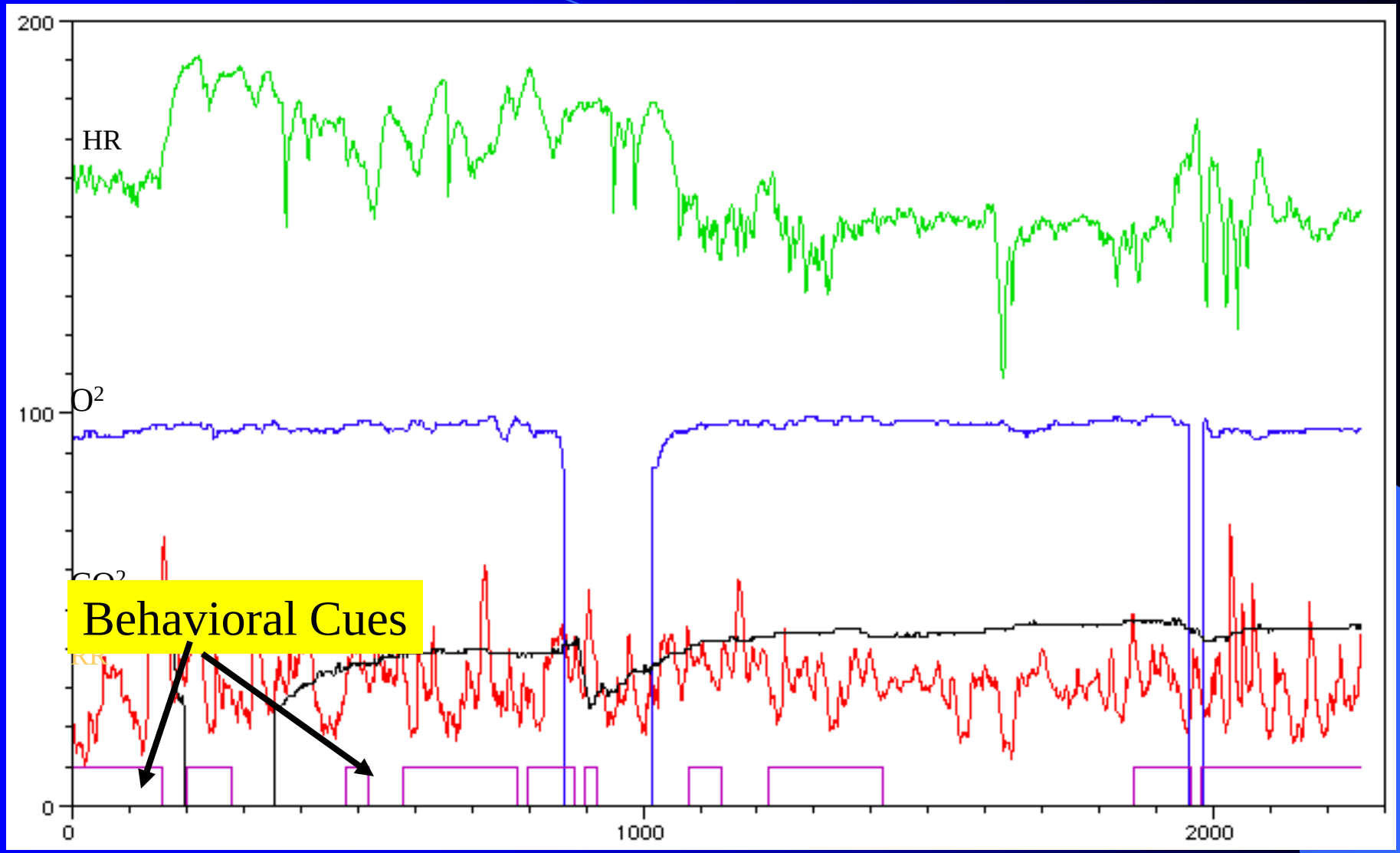
What type of mathematical representation should be considered?

When modeling time series data one needs to explicitly specify an analytic structure to the model. In many cases very little is known about the structure prior to modeling.

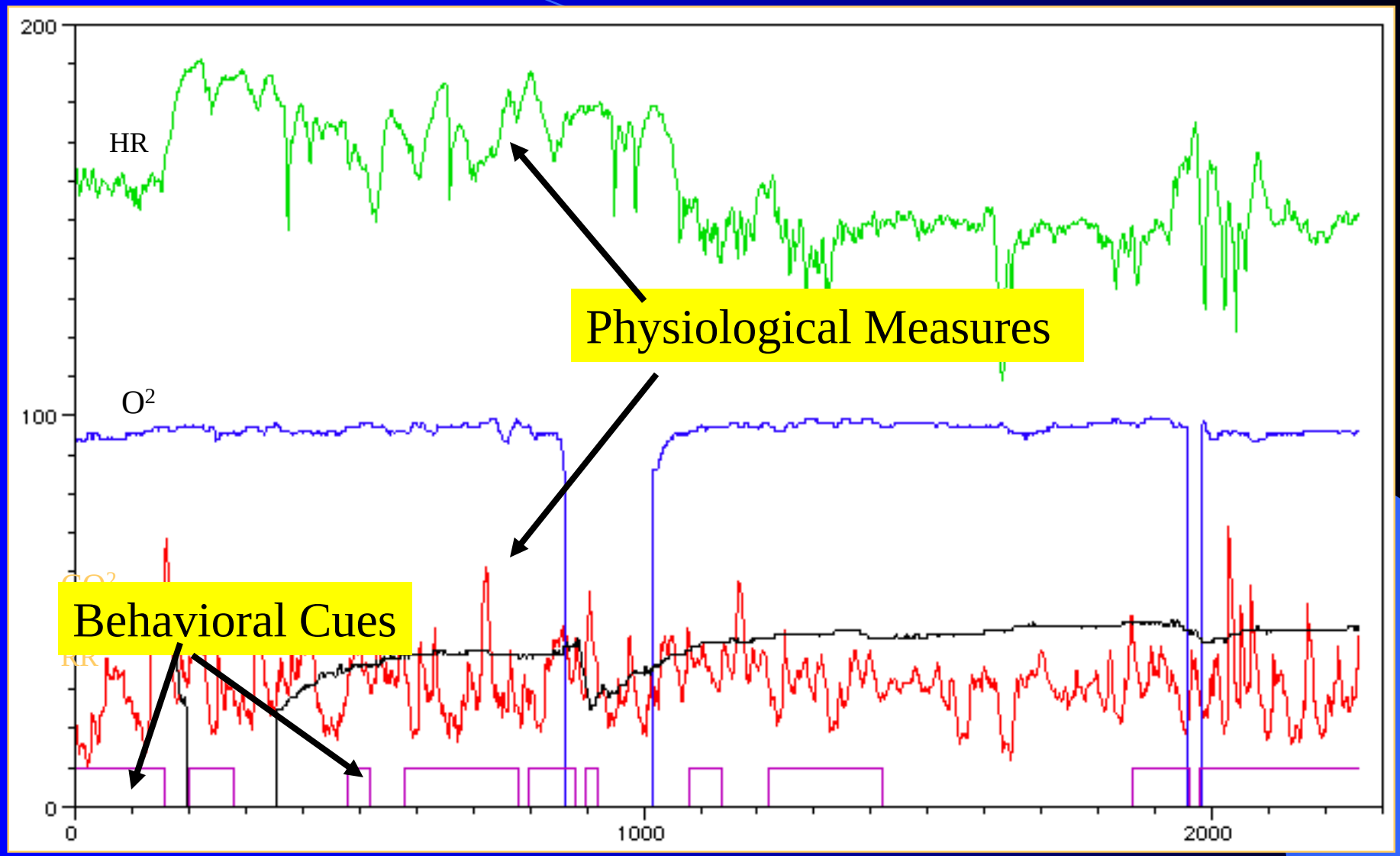
Example of A Single Nested Occasion in the Data Hierarchy



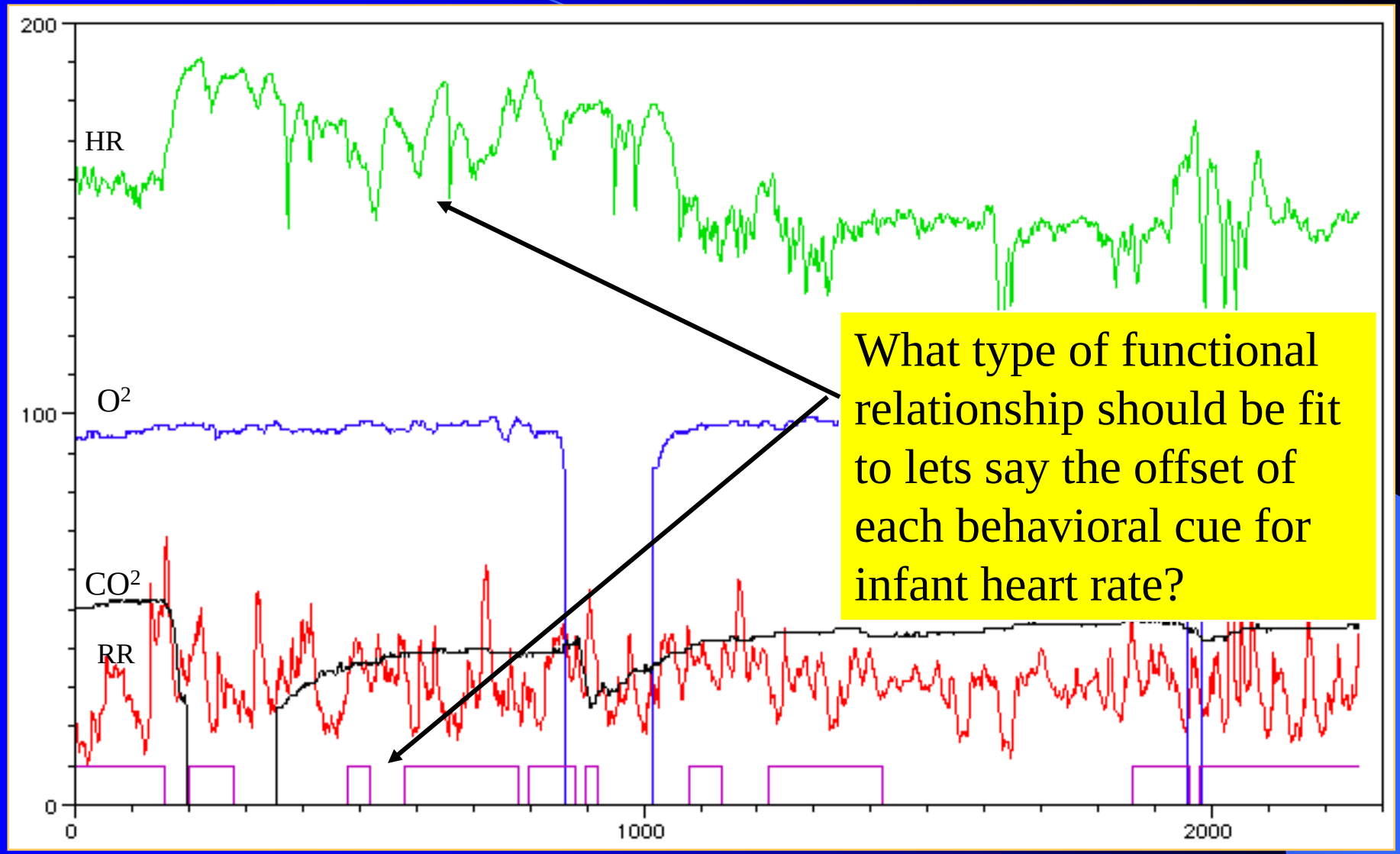
Example of A Single Nested Occasion in the Data Hierarchy



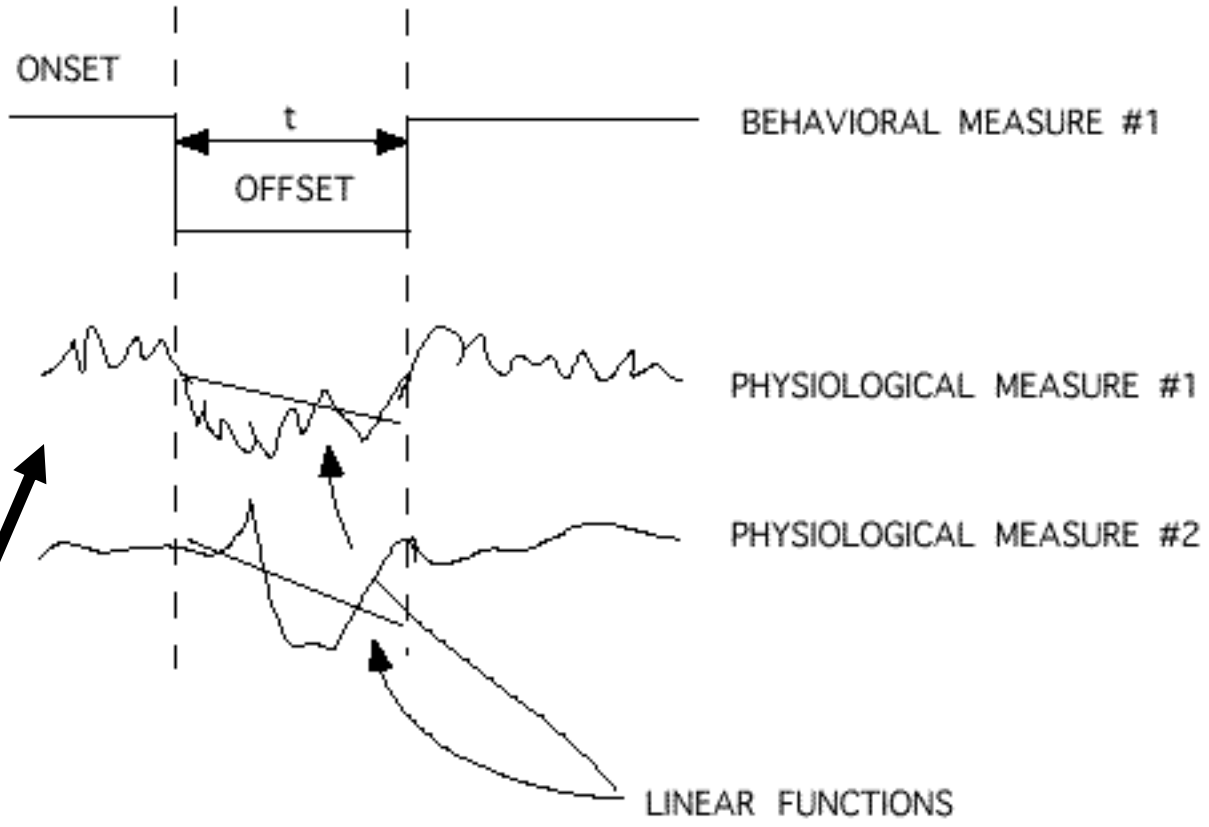
Example of A Single Nested Occasion in the Data Hierarchy



Example of A Single Nested Occasion in the Data Hierarchy



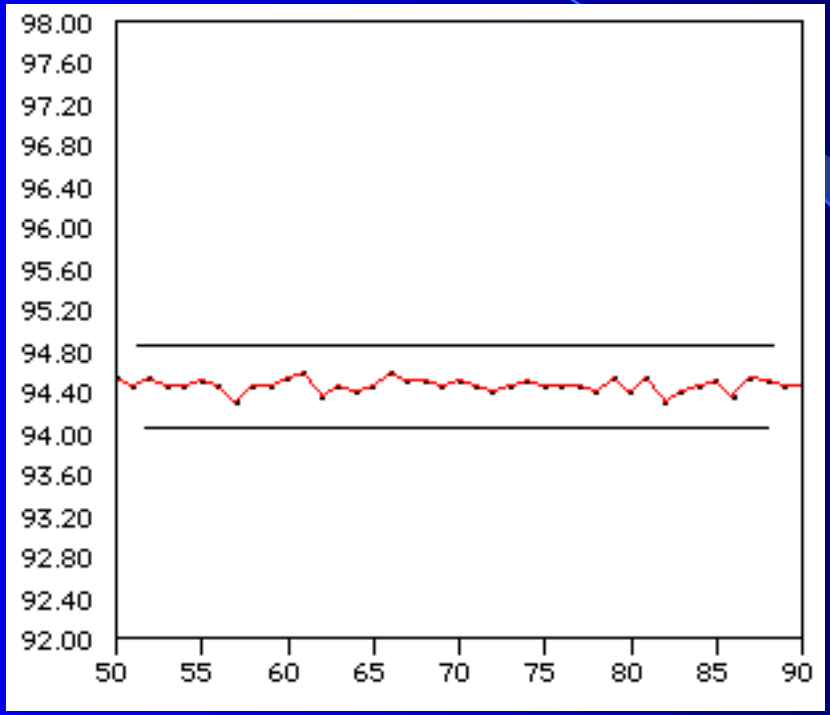
Basic Approach



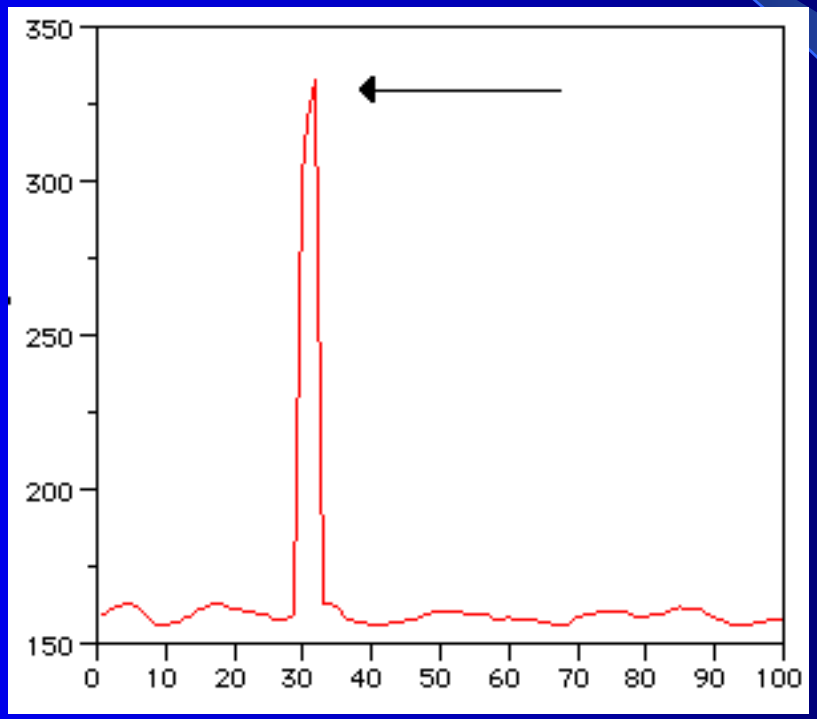
By moving to this level of the data one may better understand the relationships.

One may encounter a wide variety of conditions in the time series - for example

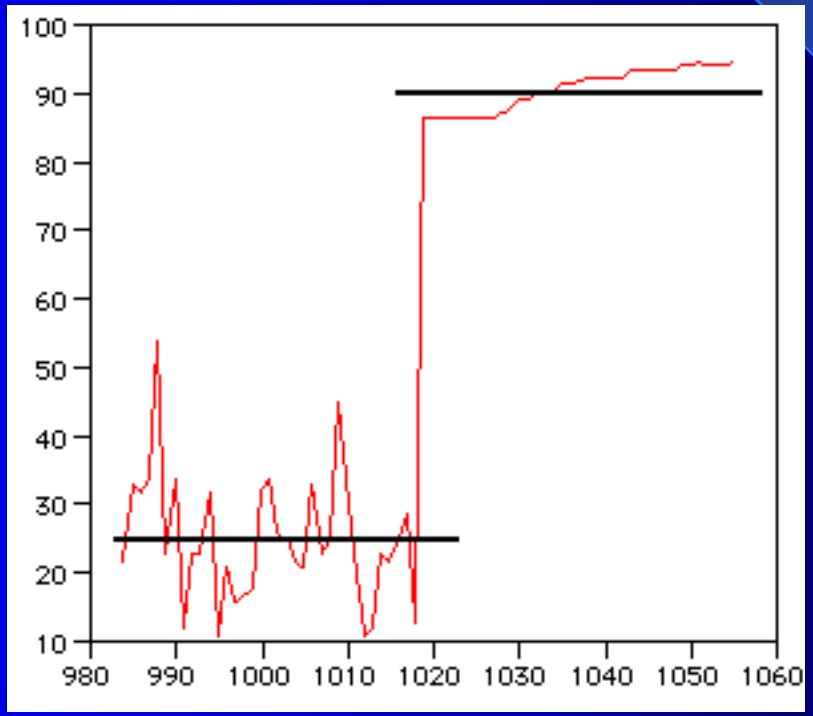
Stable State



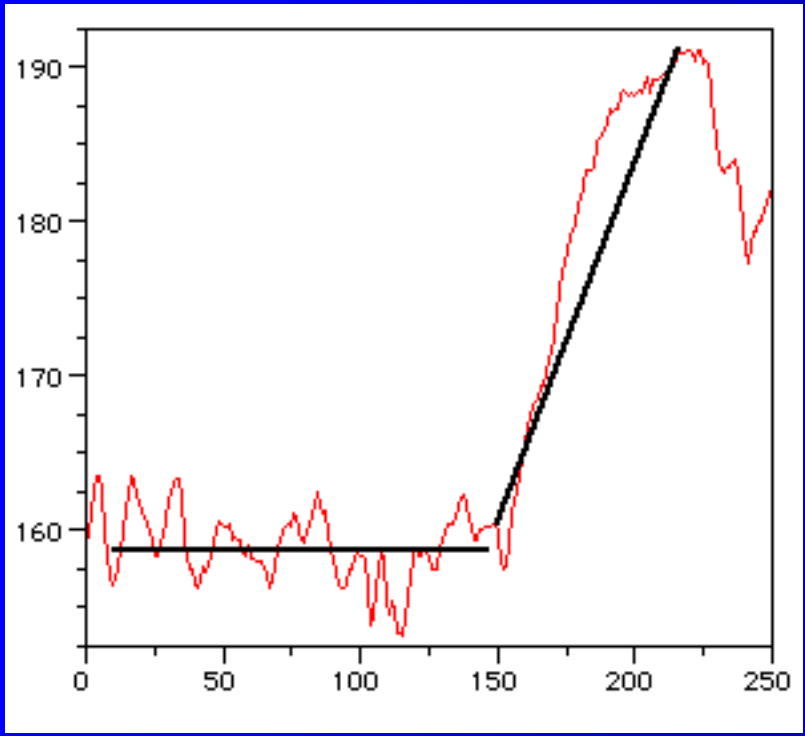
Outliers or Extreme Values

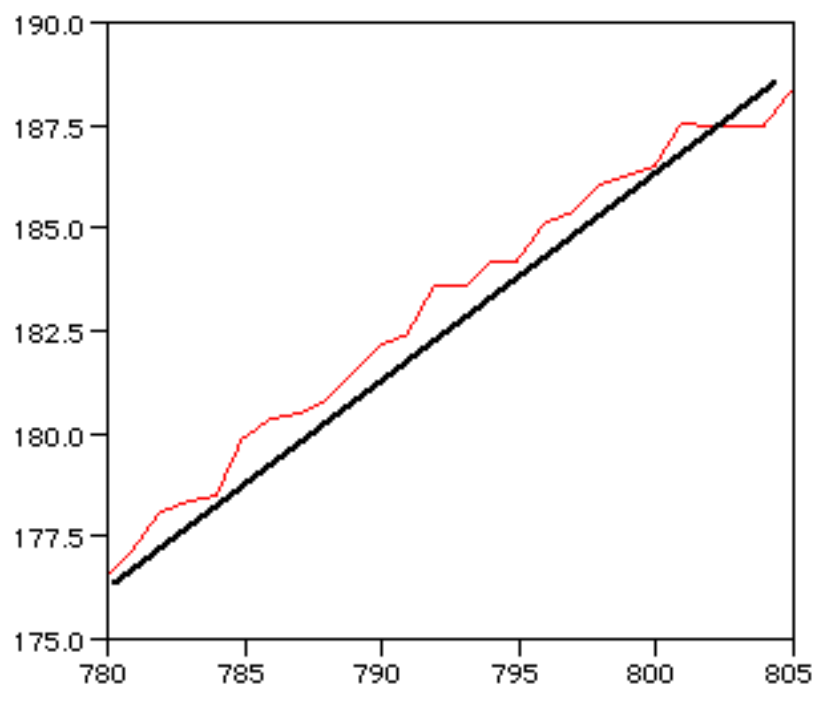


Change in Level - Abrupt

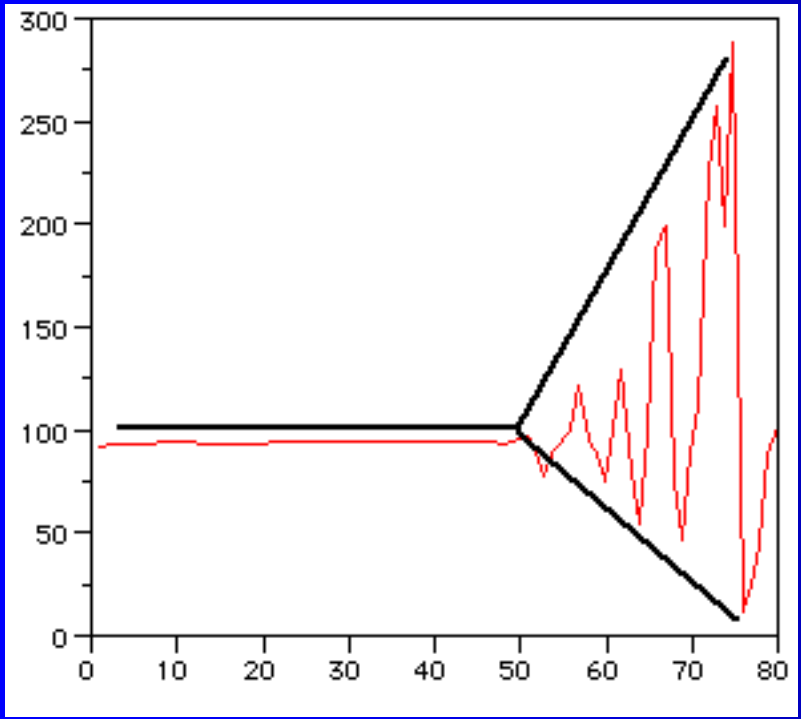


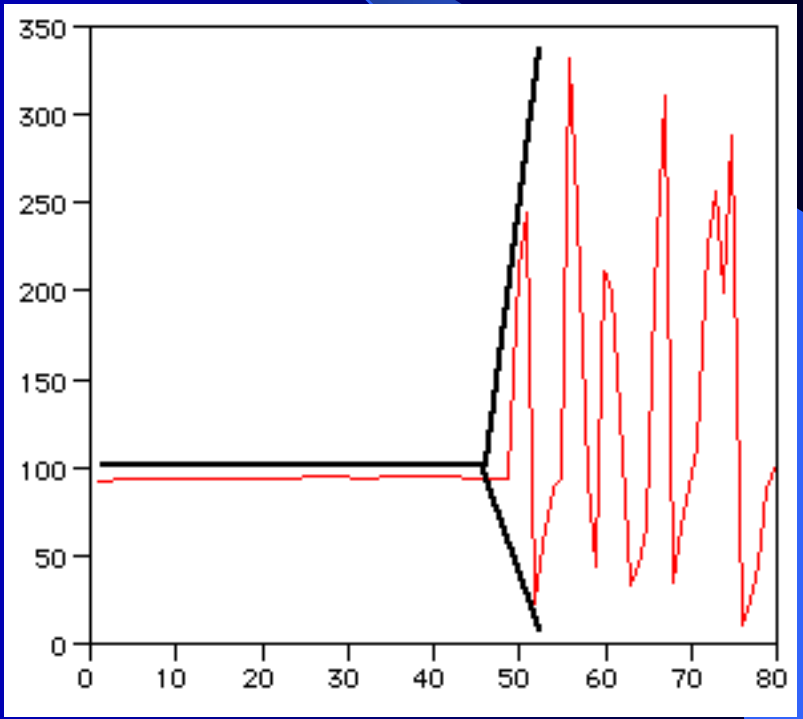
Change in Level - Gradual





Changes in Variability

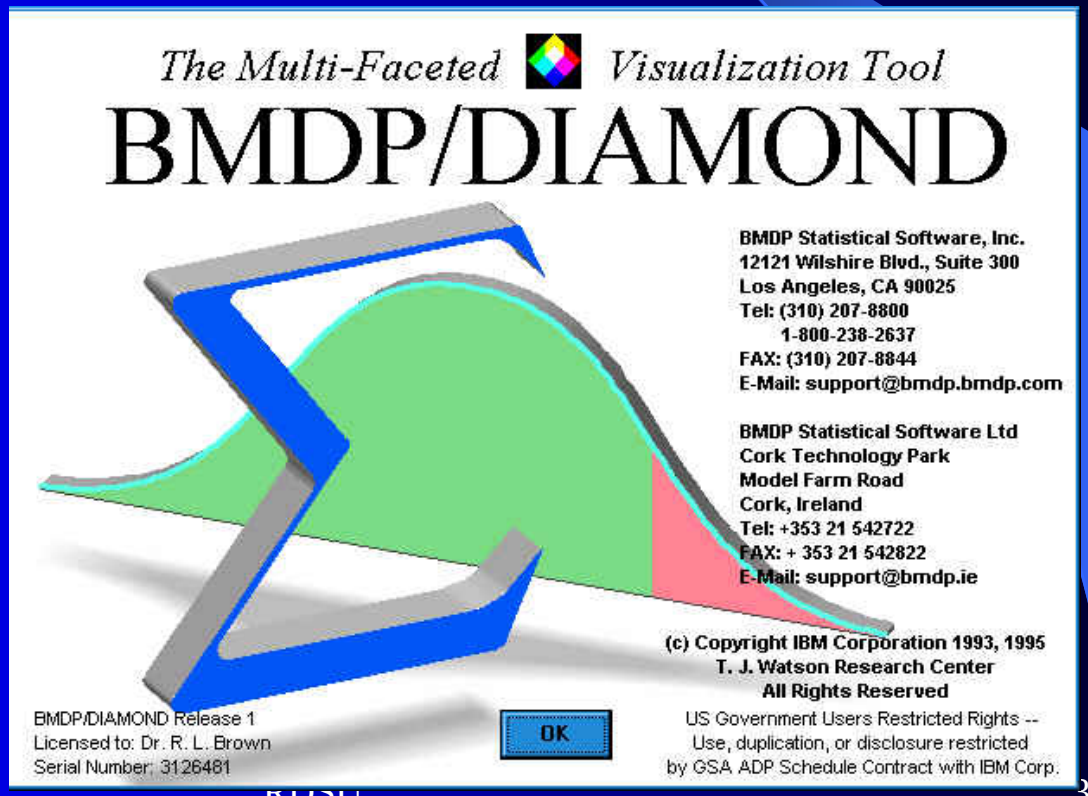


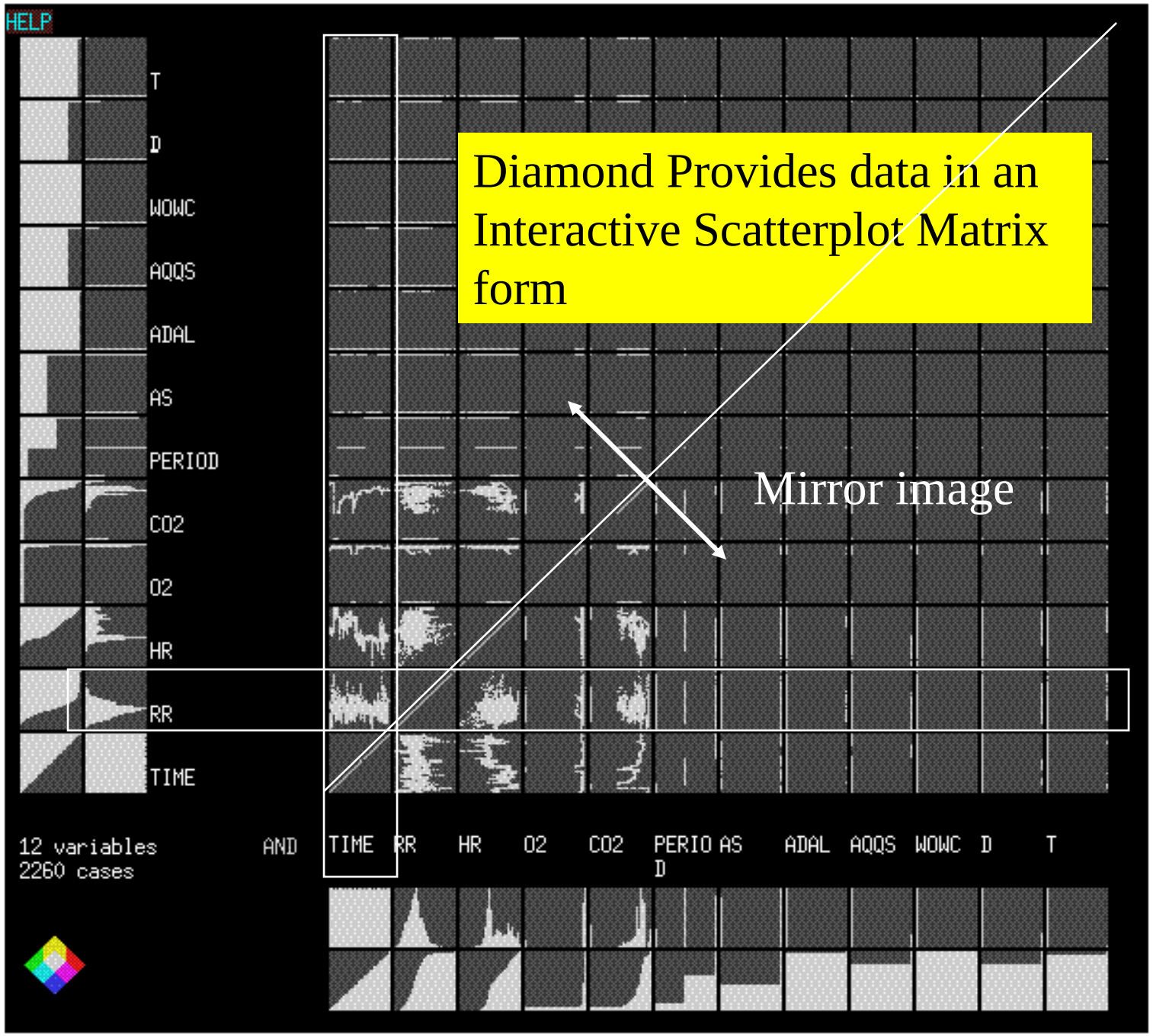


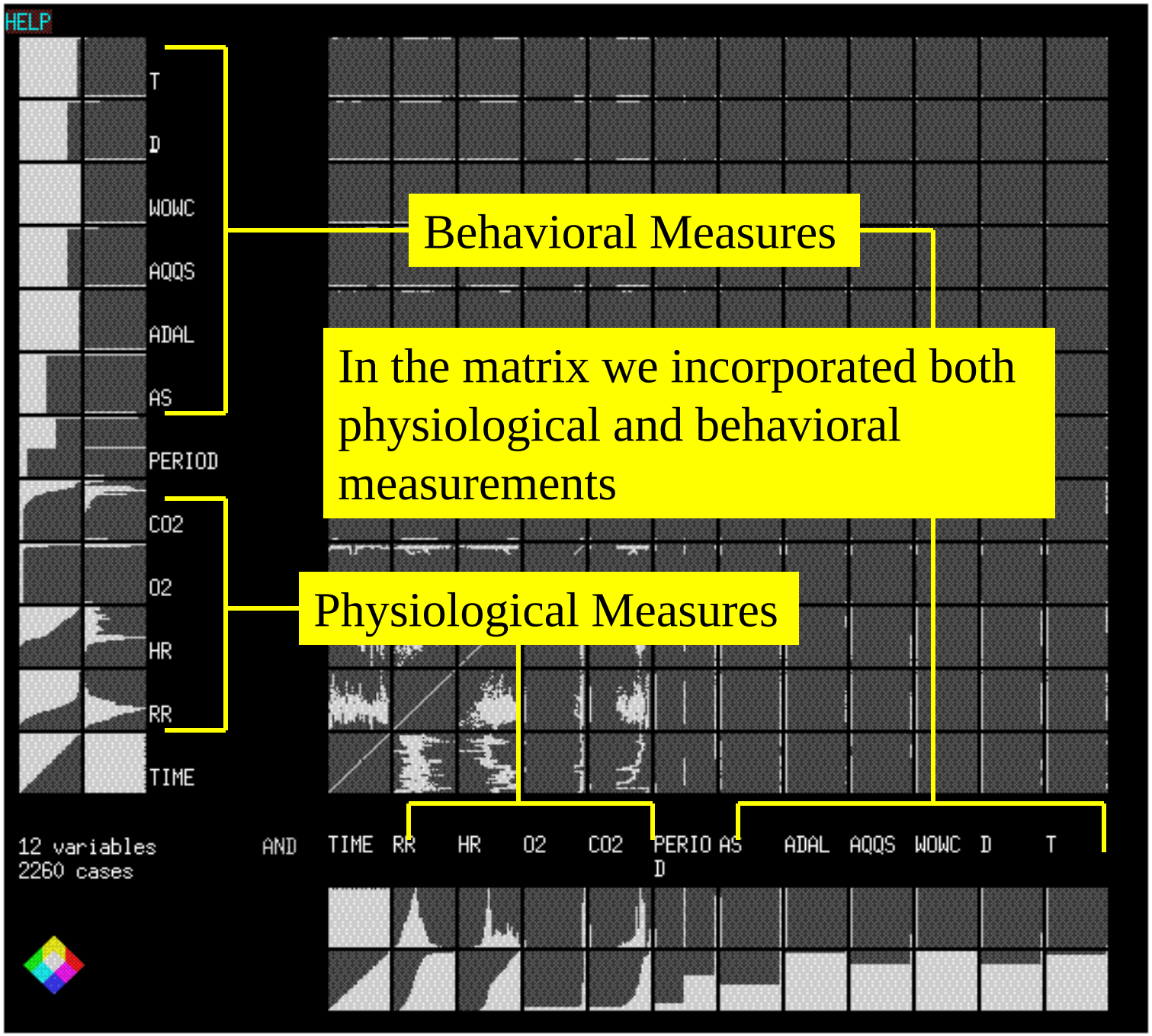
Prior to Building Our Mathematical Model we need

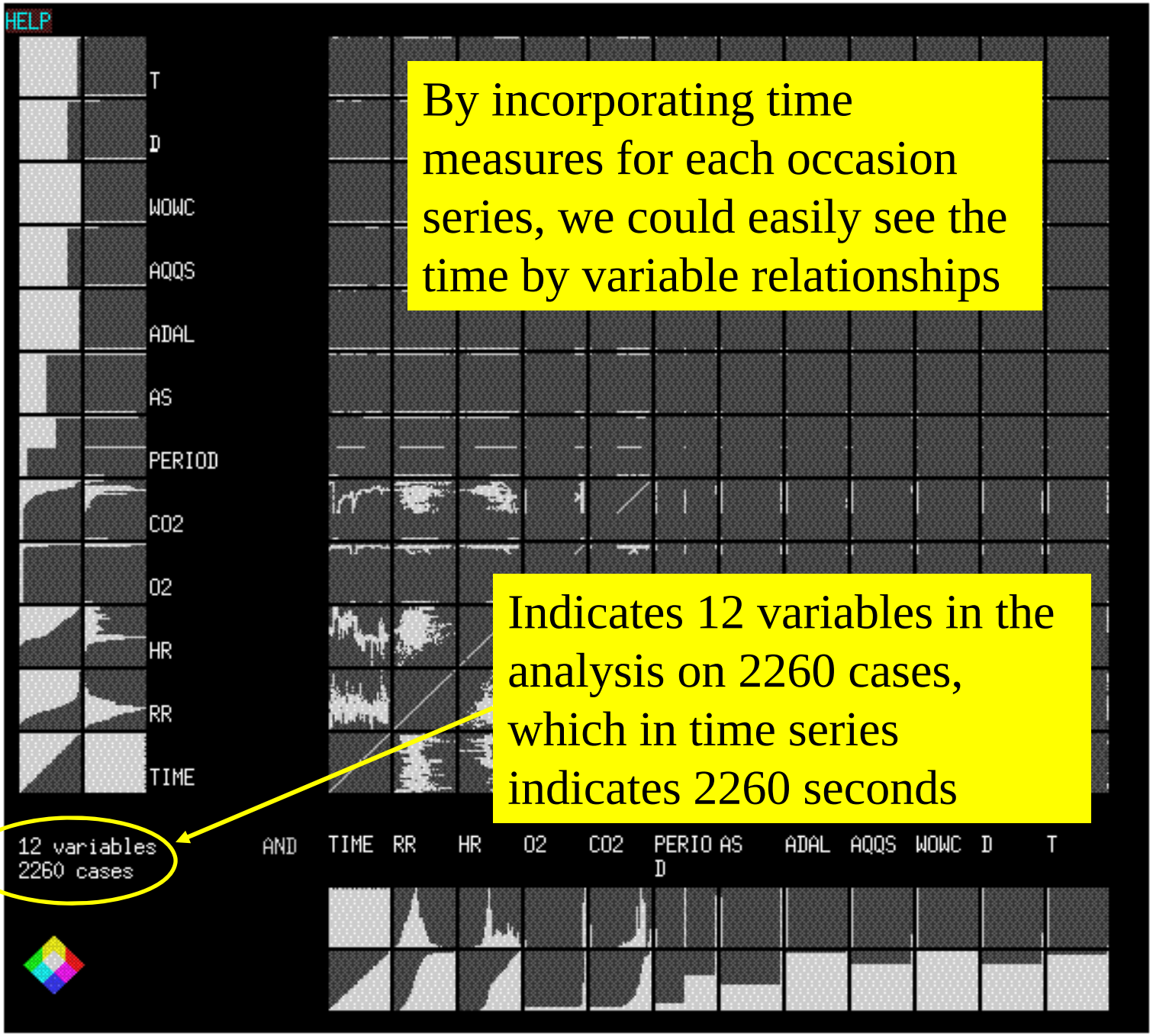
- A system that could handle large amounts of time-series data simultaneously
- A system that had powerful multivariate visual exploratory data capabilities
- A system that provided interactive sub-setting and linking
- A system that would allow on-the-fly function construction

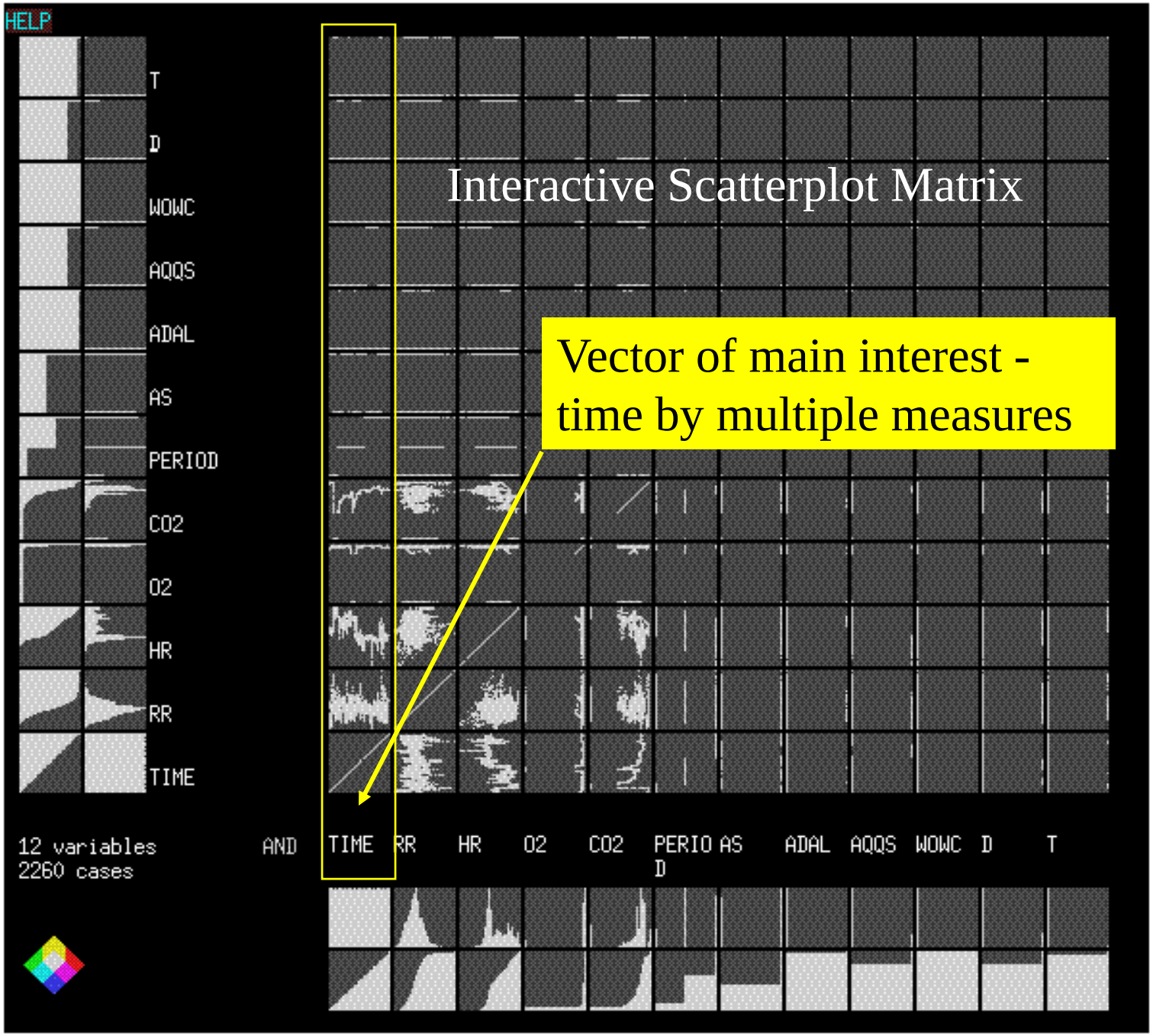
The system we chose was Diamond, now marketed by SPSS. This system provided all the requirements necessary for understanding sub-setted functional relationships.

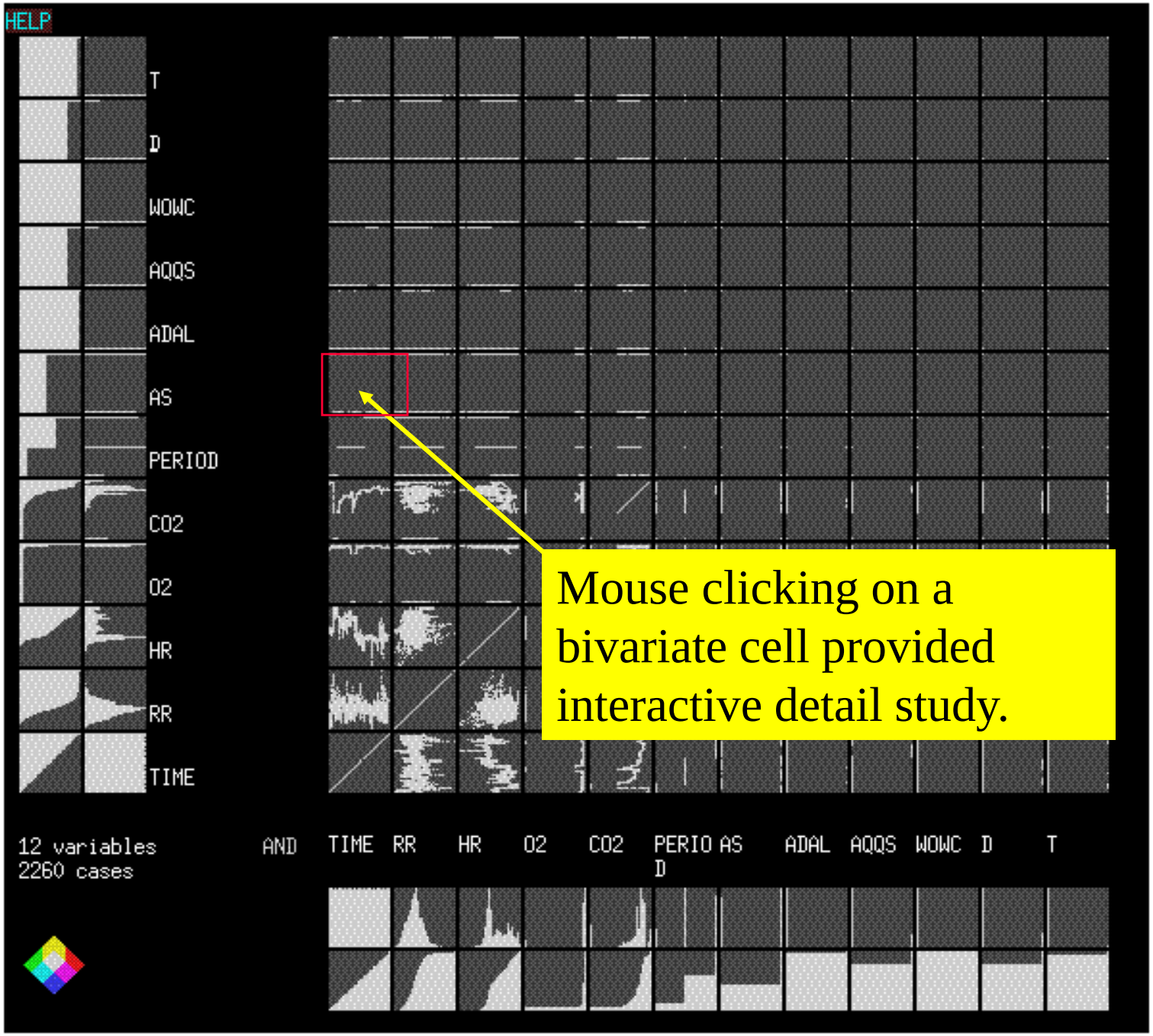


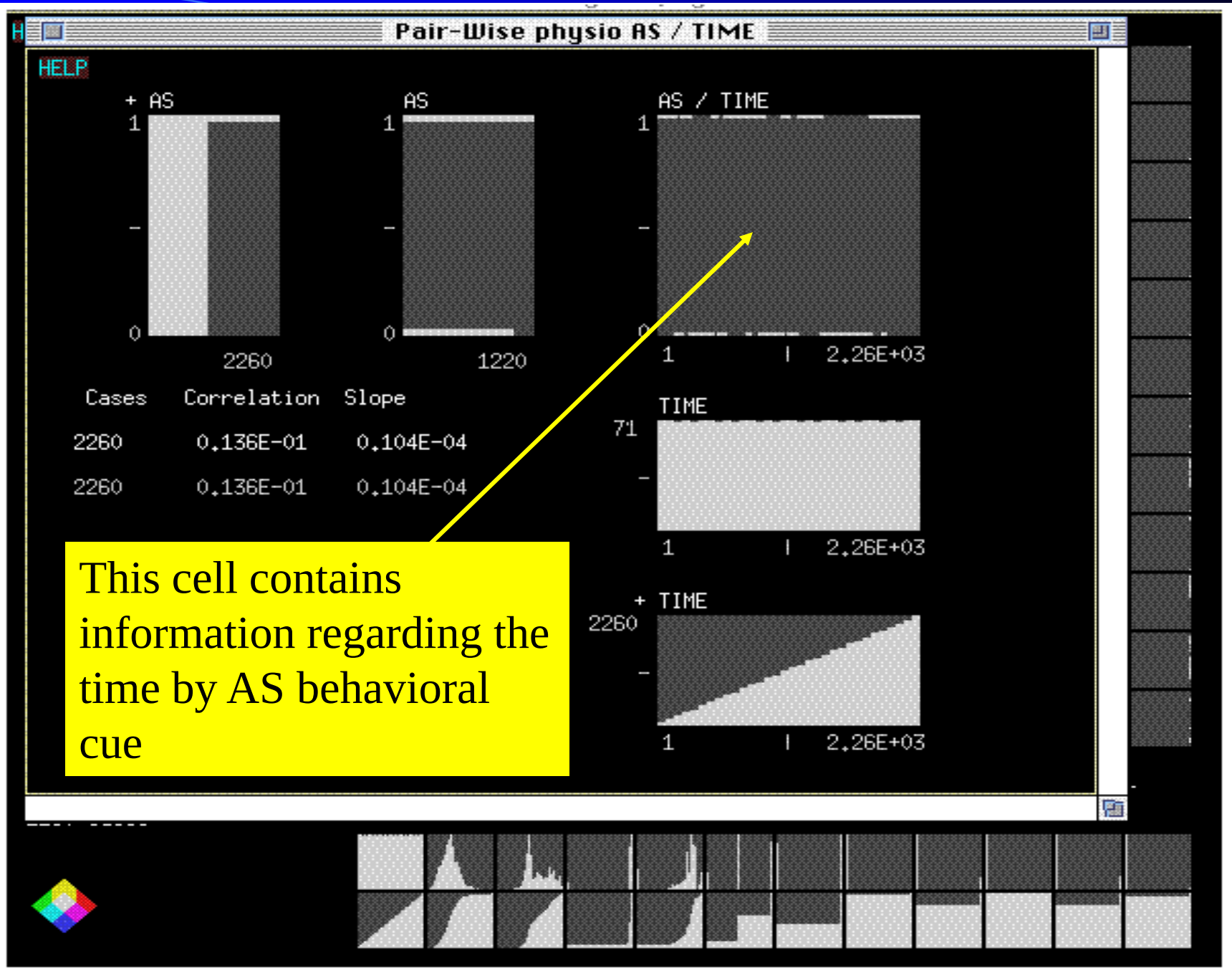

HELP
T
D
WOWC
AQQS
ADAL
AS
PERIOD
CO2
O2
HR
RR
TIME
Diamond Provides data in an Interactive Scatterplot Matrix form
Mirror image
12 variables
2260 cases
AND
TIME
RR
HR
O2
CO2
PERIO D
AS
ADAL
AQQS
WOWC
D
T

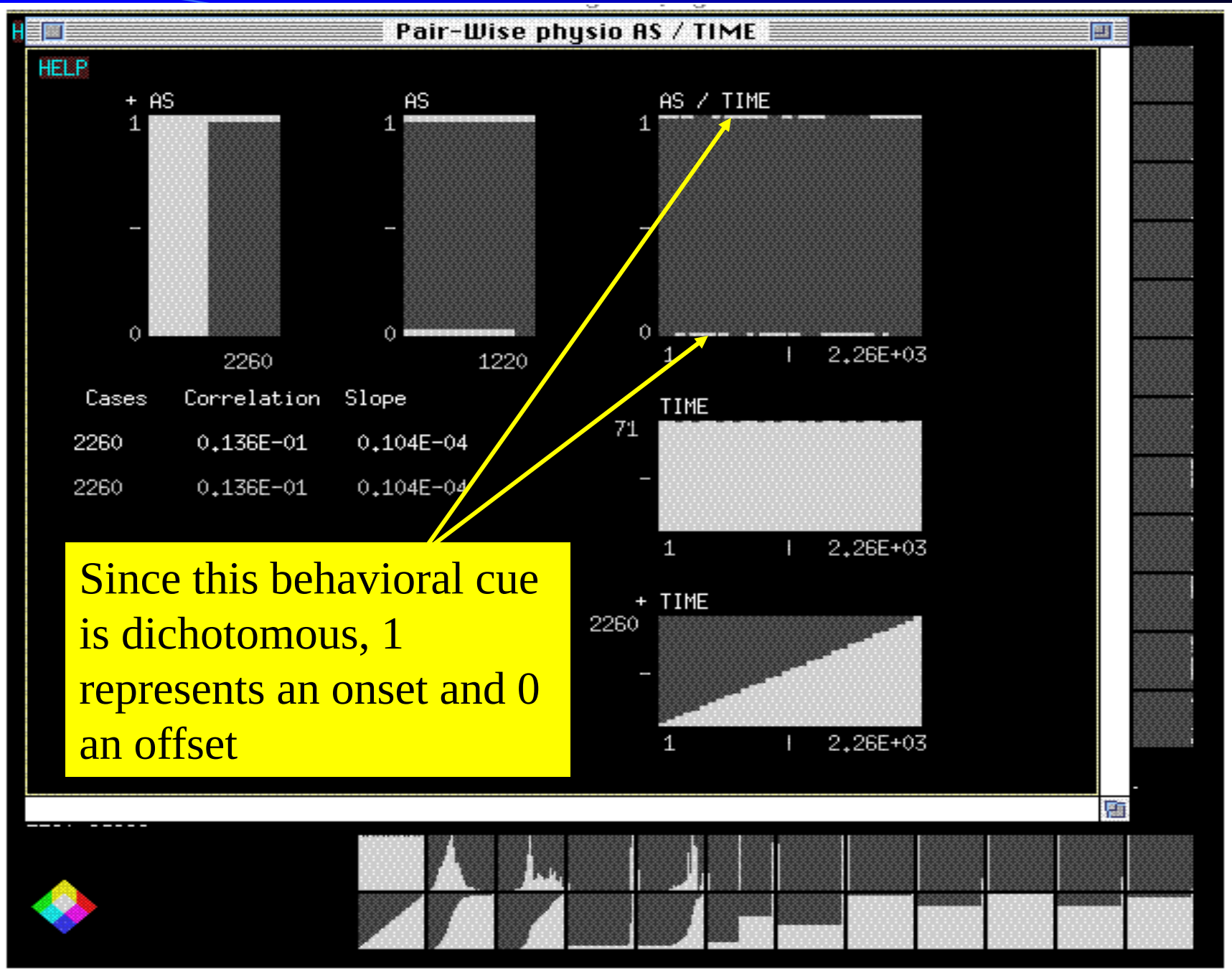

HELP
T
D
WOWC
AQQS
ADAL
AS
PERIOD
CO2
O2
HR
RR
TIME
Behavioral Measures
In the matrix we incorporated both physiological and behavioral measurements
Physiological Measures
12 variables
2260 cases
AND
TIME RR HR O2 CO2 PERIO D AS ADAL AQQS WOWC D T

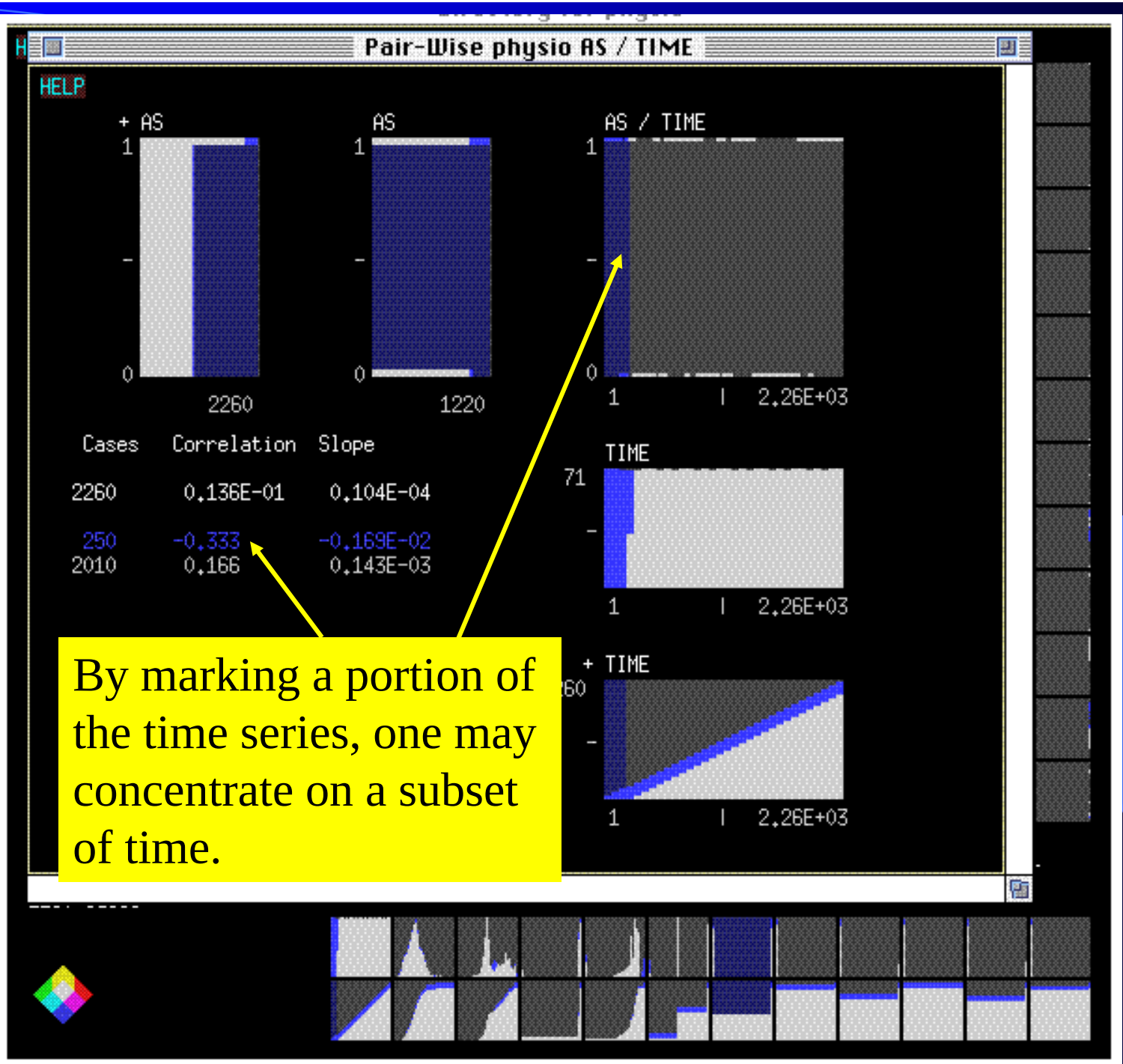

HELP
T
D
WOWC
AQQS
ADAL
AS
PERIOD
CO2
O2
HR
RR
TIME
By incorporating time measures for each occasion series, we could easily see the time by variable relationships
Indicates 12 variables in the analysis on 2260 cases, which in time series indicates 2260 seconds
12 variables
2260 cases
AND TIME RR HR O2 CO2 PERIO AS ADAL AQQS WOWC D T
D

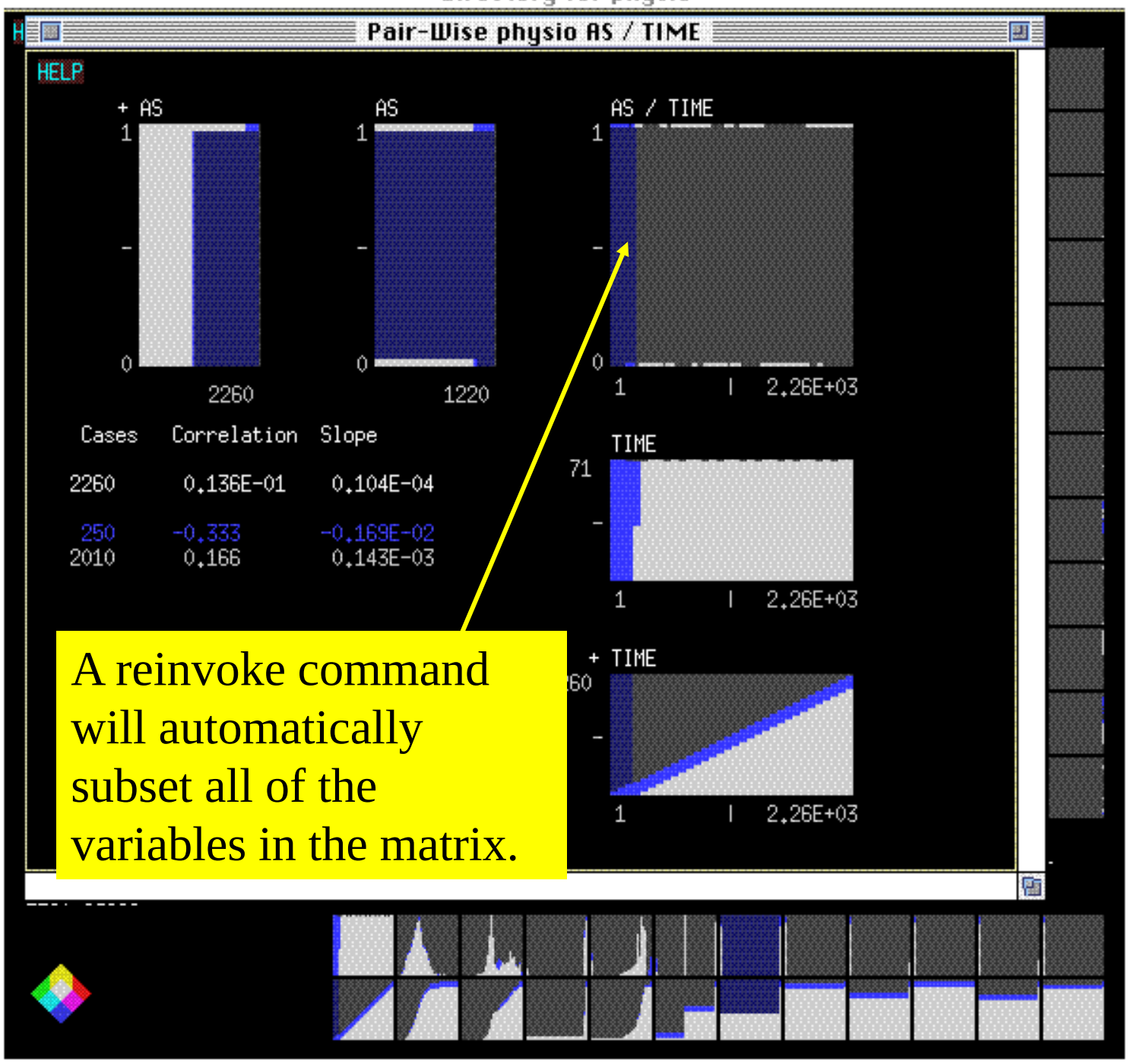

HELP
T
D
WOWC
AQQS
ADAL
AS
PERIOD
CO2
O2
HR
RR
TIME
Interactive Scatterplot Matrix
Vector of main interest - time by multiple measures
12 variables
2260 cases
AND
TIME
RR
HR
O2
CO2
PERIO D
AS
ADAL
AQQS
WOWC
D
T


HELP
T
D
WOWC
AQQS
ADAL
AS
PERIOD
CO2
O2
HR
RR
TIME
Mouse clicking on a bivariate cell provided interactive detail study.
12 variables
2260 cases
AND
TIME RR HR O2 CO2 PERIO AS ADAL AQQS WOWC D T
D

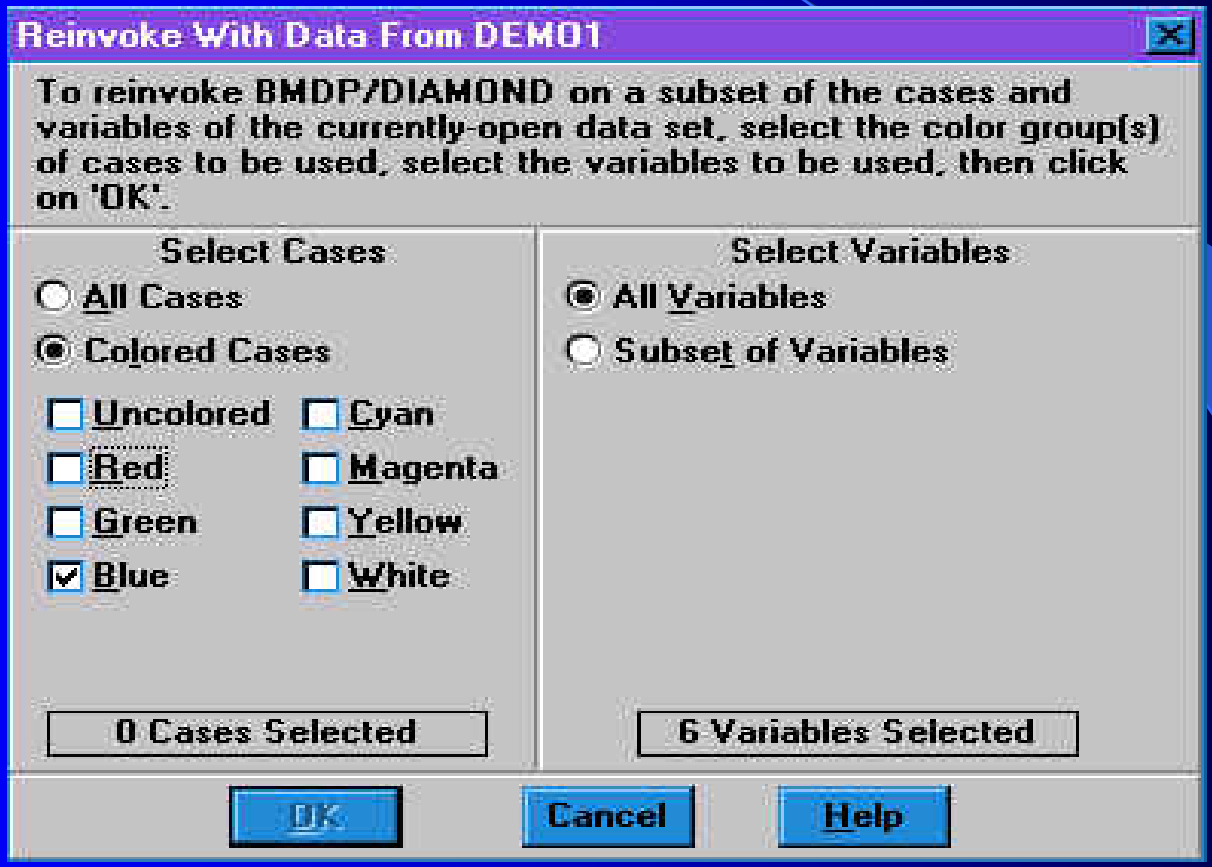

Pair-Wise physio AS / TIME
HELP
+ AS
1
0
2260
AS
1
0
1220
AS / TIME
1
0
1
2.26E+03
Cases
Correlation
Slope
2260
0.136E-01
0.104E-04
2260
0.136E-01
0.104E-04
TIME
71
1
2.26E+03
+ TIME
2260
1
2.26E+03
This cell contains information regarding the time by AS behavioral cue

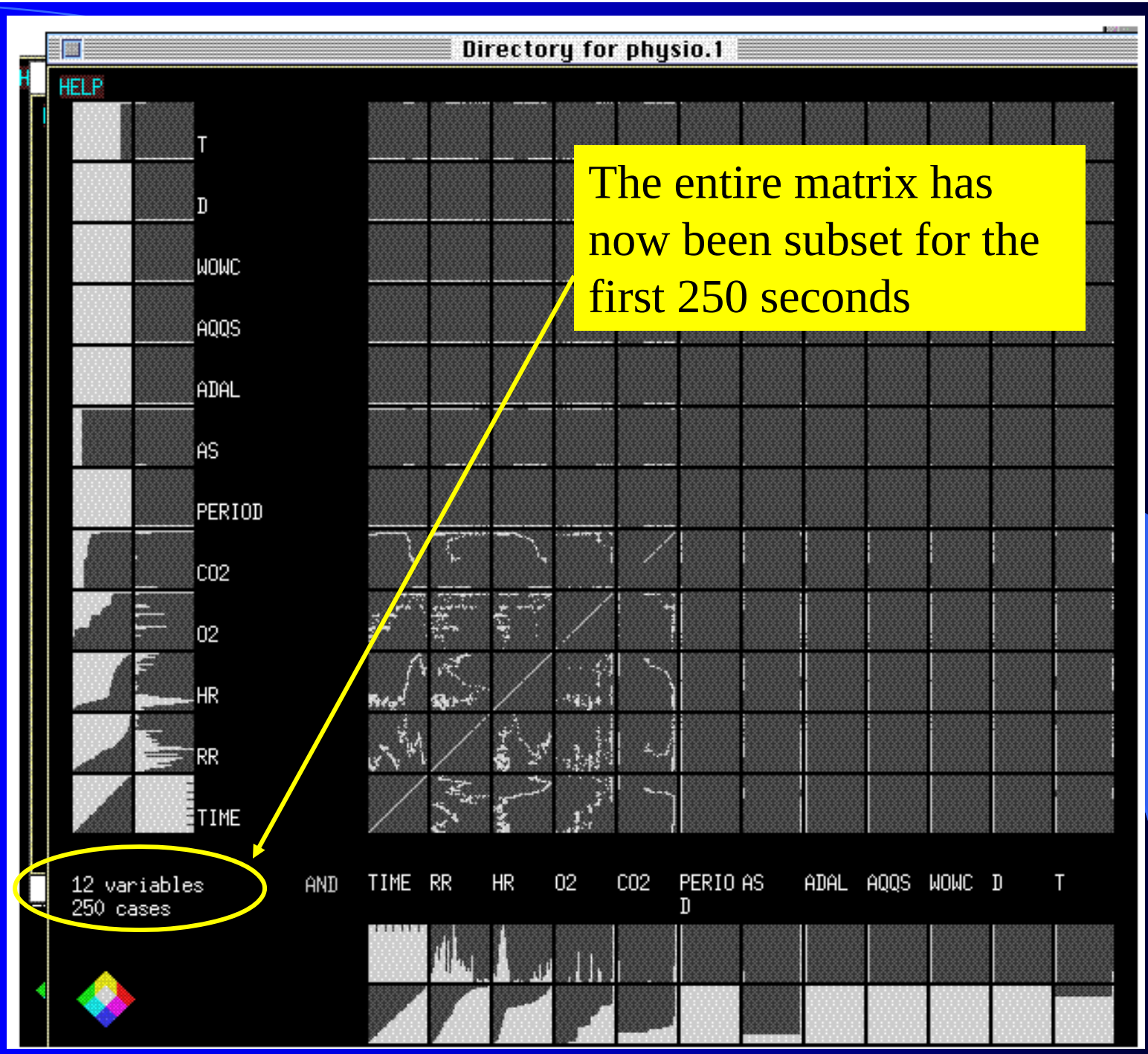

Pair-Wise physio AS / TIME
HELP
+ AS
1
0
2260
AS
1
0
1220
AS / TIME
1
0
1
2.26E+03
Cases
Correlation
Slope
2260
0.136E-01
0.104E-04
2260
0.136E-01
0.104E-04
TIME
71
1
2.26E+03
+ TIME
2260
1
2.26E+03
Since this behavioral cue is dichotomous, 1 represents an onset and 0 an offset

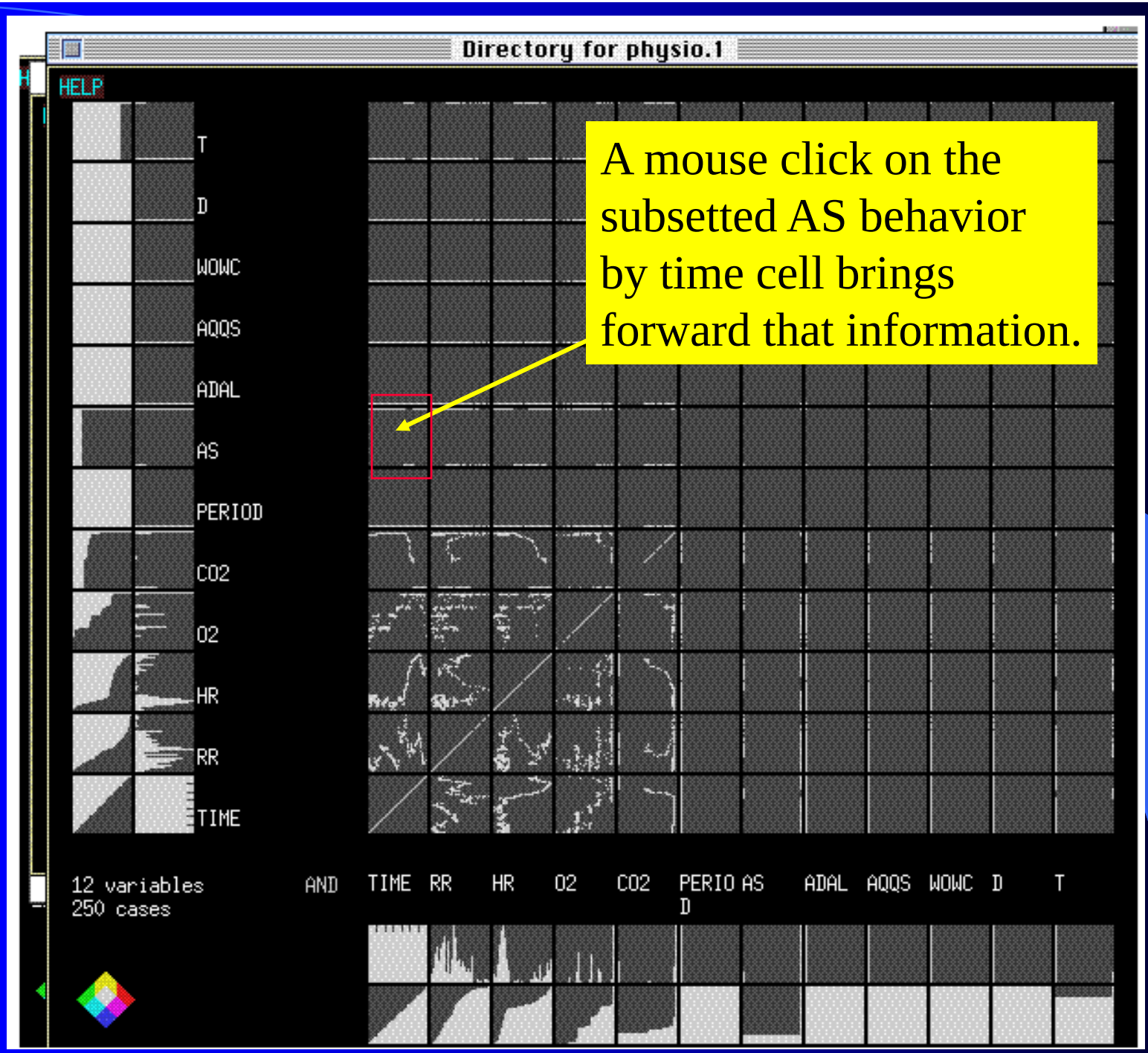

Pair-Wise physio AS / TIME
HELP
+ AS
1
0
2260
AS
1
0
1220
AS / TIME
1
0
1
2.26E+03
Cases
Correlation
Slope
2260
0.136E-01
0.104E-04
250
-0.333
-0.169E-02
2010
0.166
0.143E-03
TIME
71
1
2.26E+03
+ TIME
1
2.26E+03
By marking a portion of the time series, one may concentrate on a subset of time.

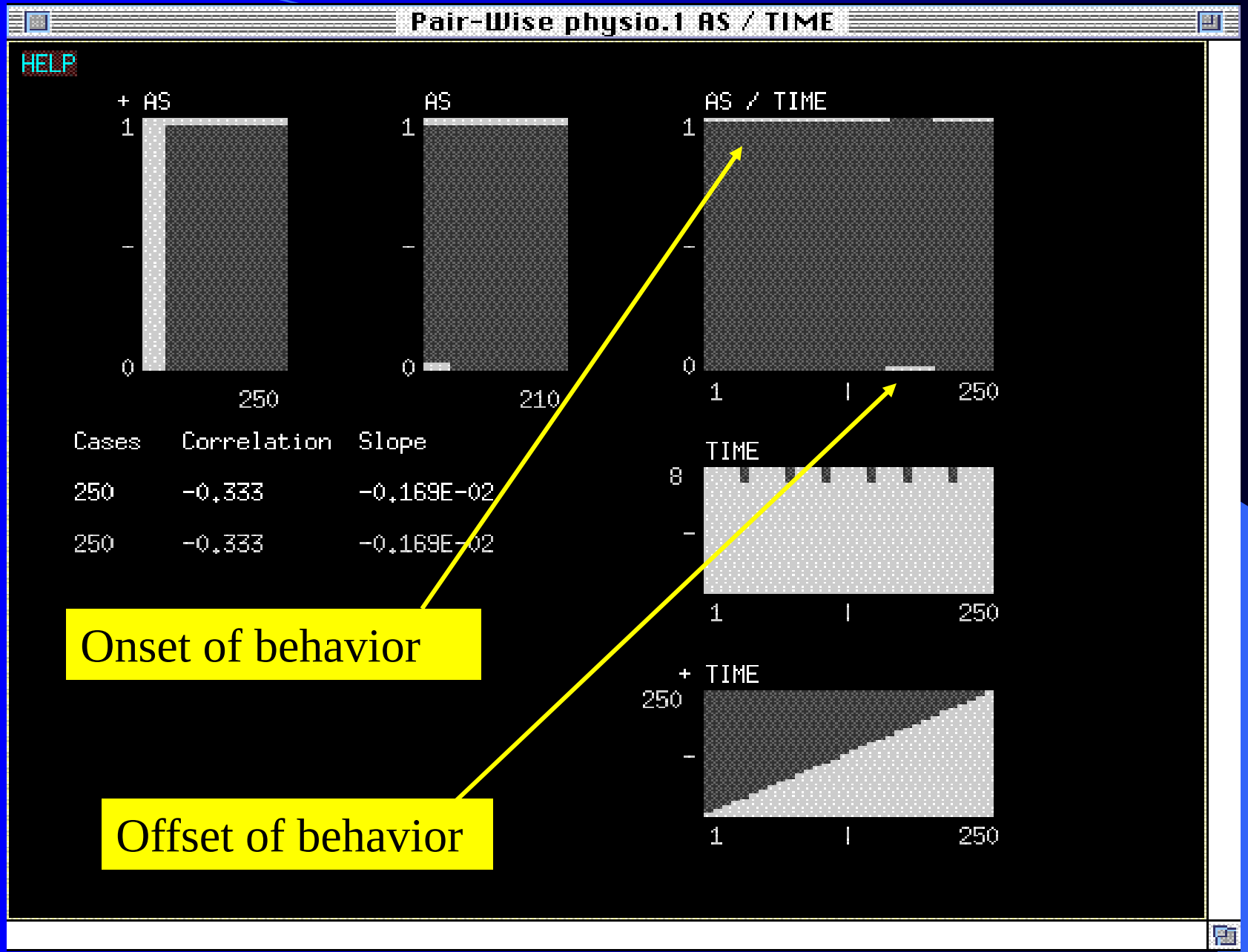

Pair-Wise physio AS / TIME
HELP
+ AS
1
0
2260
AS
1
0
1220
AS / TIME
1
0
1
2.26E+03
Cases
Correlation
Slope
2260
0.136E-01
0.104E-04
250
-0.333
-0.169E-02
2010
0.166
0.143E-03
TIME
71
1
2.26E+03
+ TIME
1
2.26E+03
A reinvoke command will automatically subset all of the variables in the matrix.

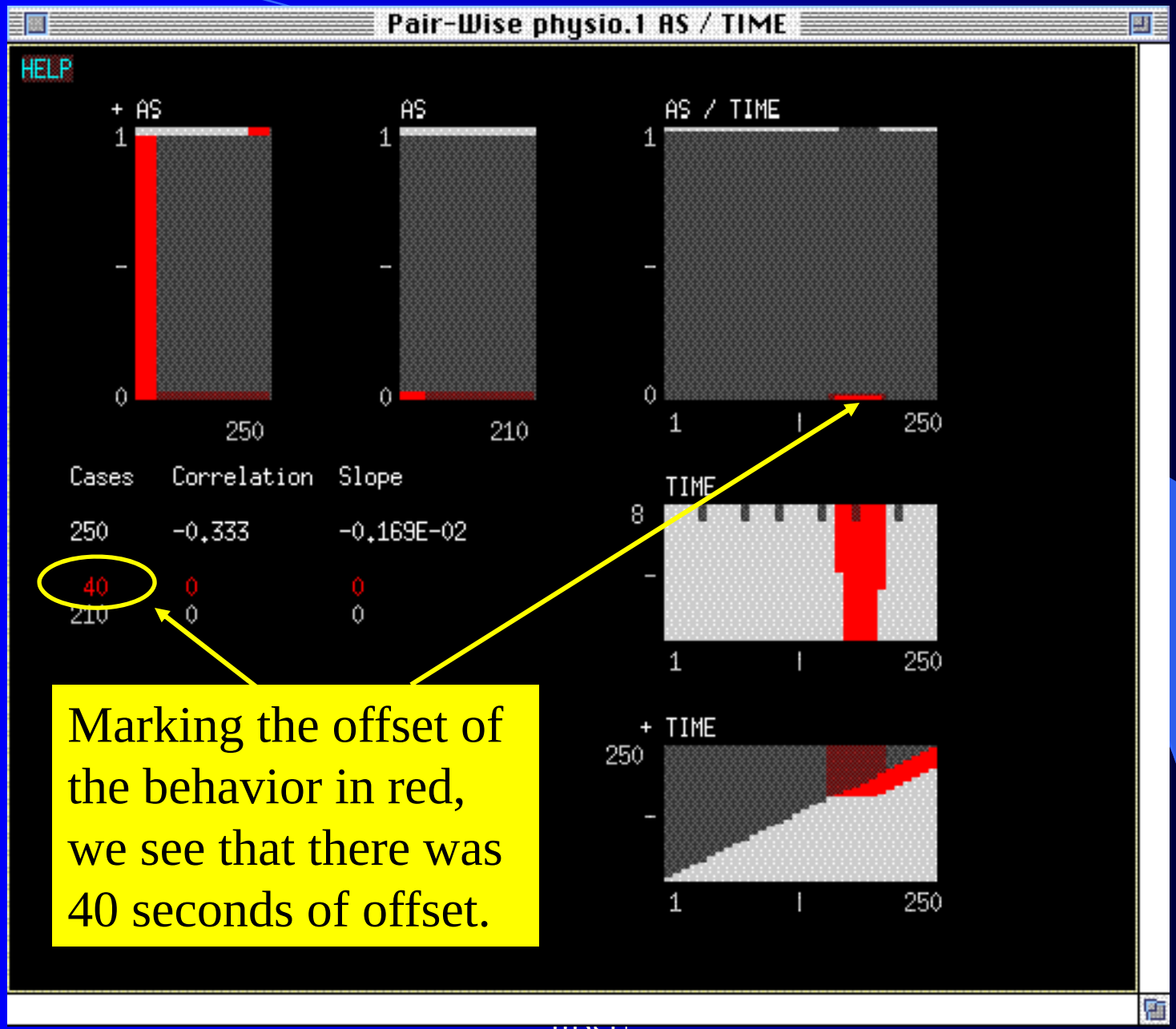
Example of the Diamond Reinvoke Window

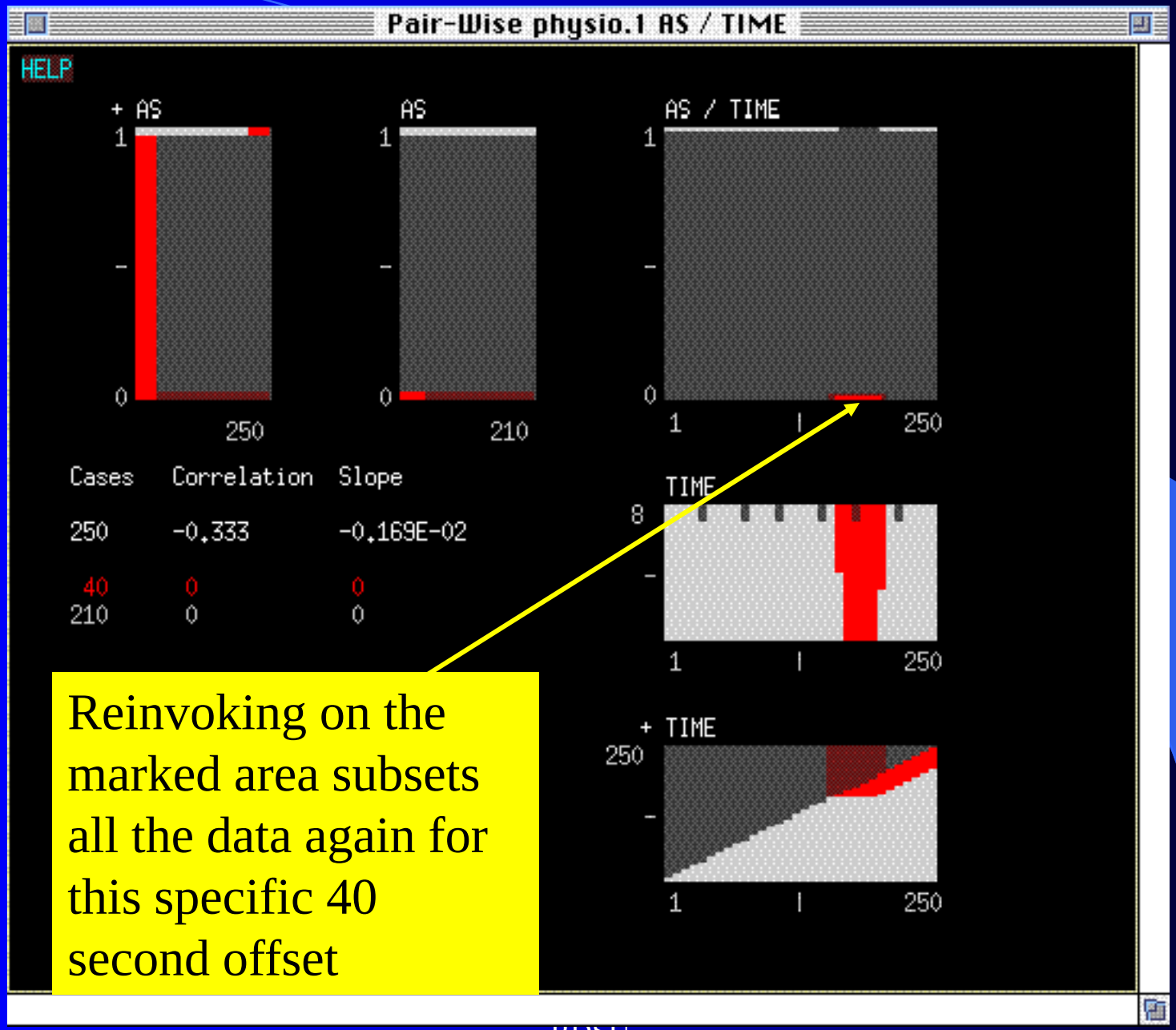


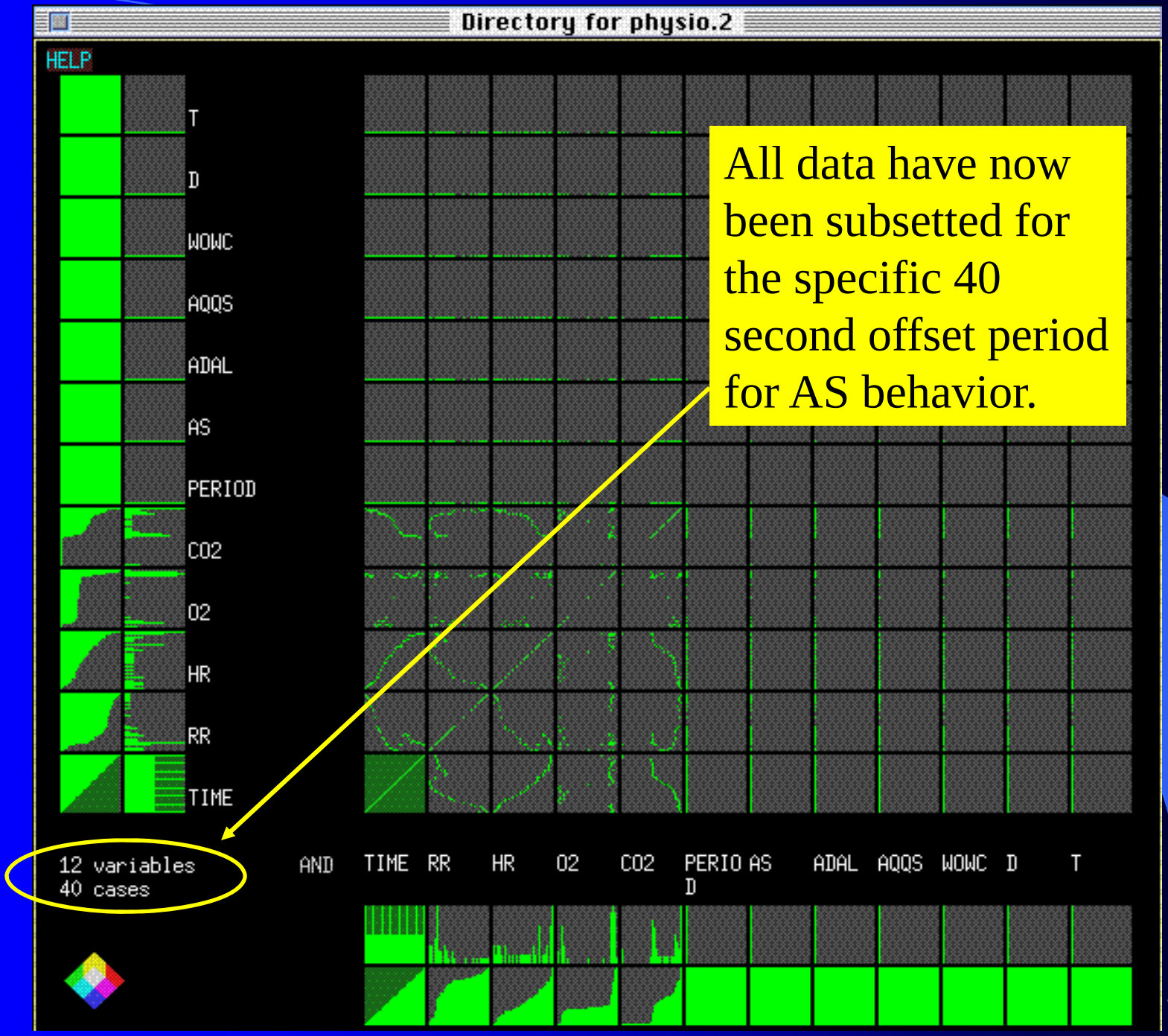

Directory for physio.1
HELP
T
D
WOWC
AQQS
ADAL
AS
PERIOD
CO2
O2
HR
RR
TIME
The entire matrix has now been subset for the first 250 seconds
12 variables
250 cases
AND
TIME RR HR O2 CO2 PERIO D AS ADAL AQQS WOWC D T

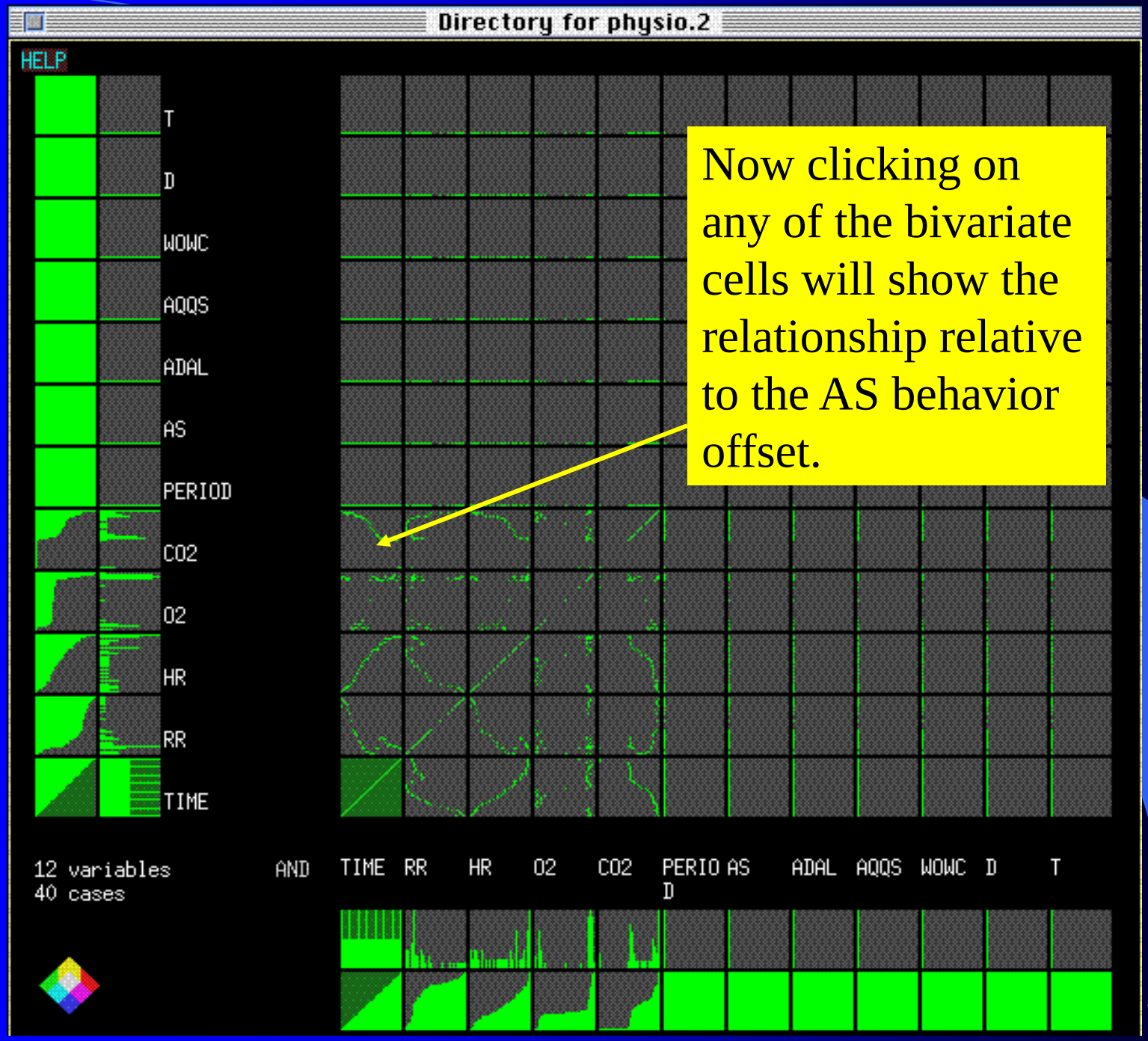

Directory for physio.1
HELP
T
D
WOWC
AQQS
ADAL
AS
PERIOD
CO2
O2
HR
RR
TIME
A mouse click on the subsetted AS behavior by time cell brings forward that information.
12 variables
250 cases
AND
TIME RR HR O2 CO2 PERIO AS ADAL AQQS WOWC D T
D

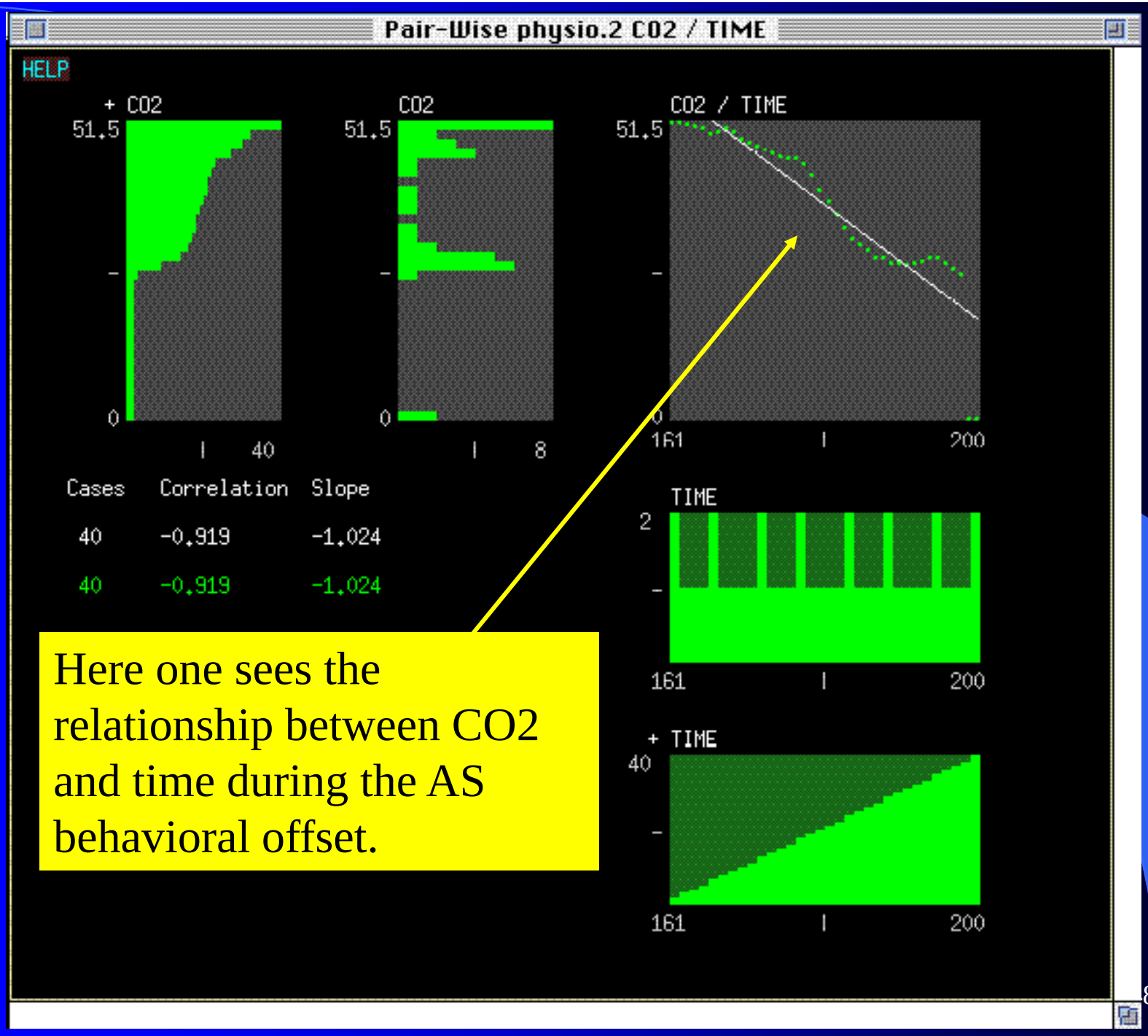

Pair-Wise physio.1 AS / TIME
HELP
+ AS
1
0
250
AS
1
0
210
AS / TIME
1
0
1
250
Cases Correlation Slope
250 -0.333 -0.169E-02
250 -0.333 -0.169E-02
TIME
8
1
250
+ TIME
250
1
250
Onset of behavior
Offset of behavior

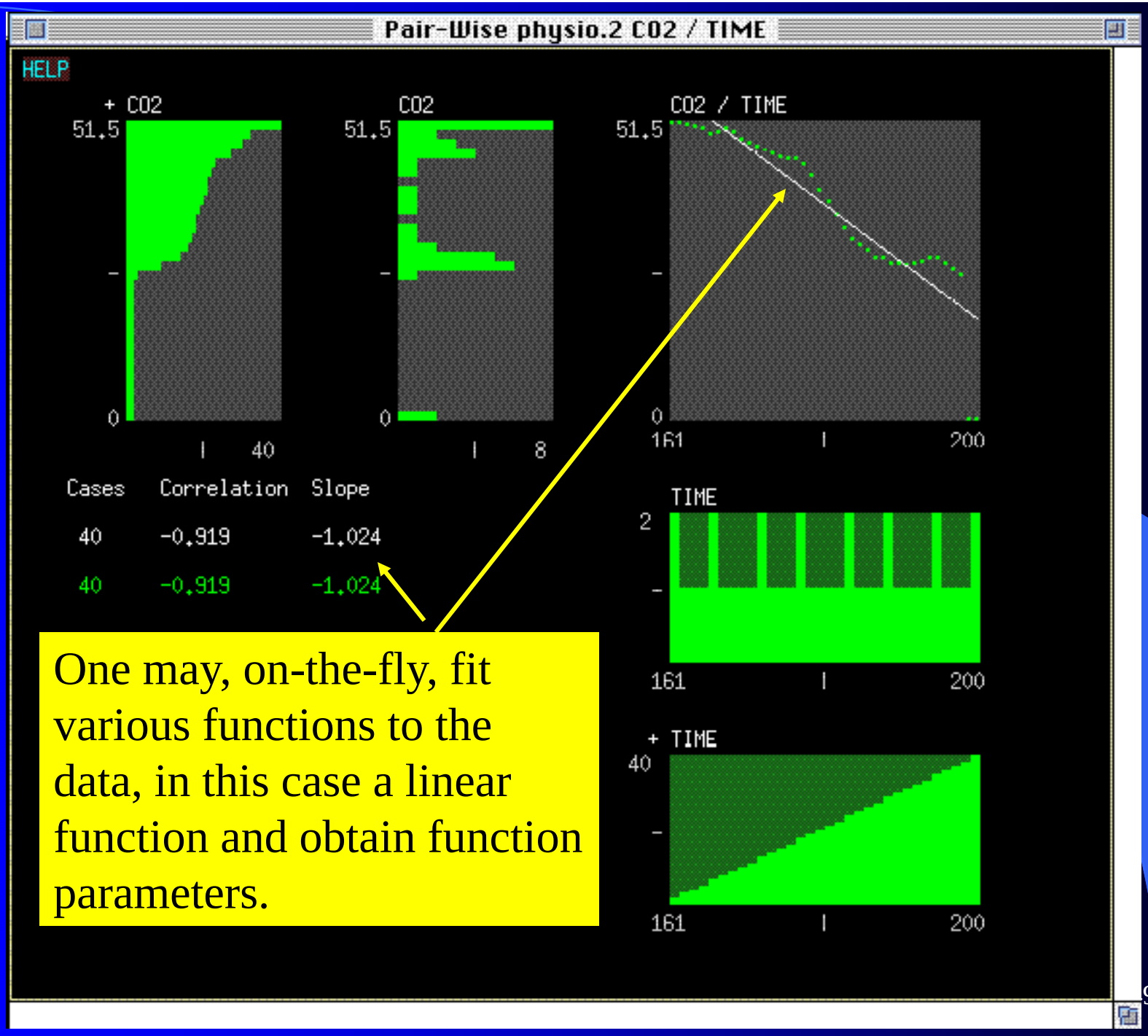

Pair-Wise physio.1 AS / TIME
HELP
+ AS
1
0
250
AS
1
0
210
AS / TIME
1
0
1
250
Cases
Correlation
Slope
250
-0,333
-0,169E-02
40
0
0
210
0
0
TIME
8
1
250
+ TIME
250
1
250
Marking the offset of the behavior in red, we see that there was 40 seconds of offset.

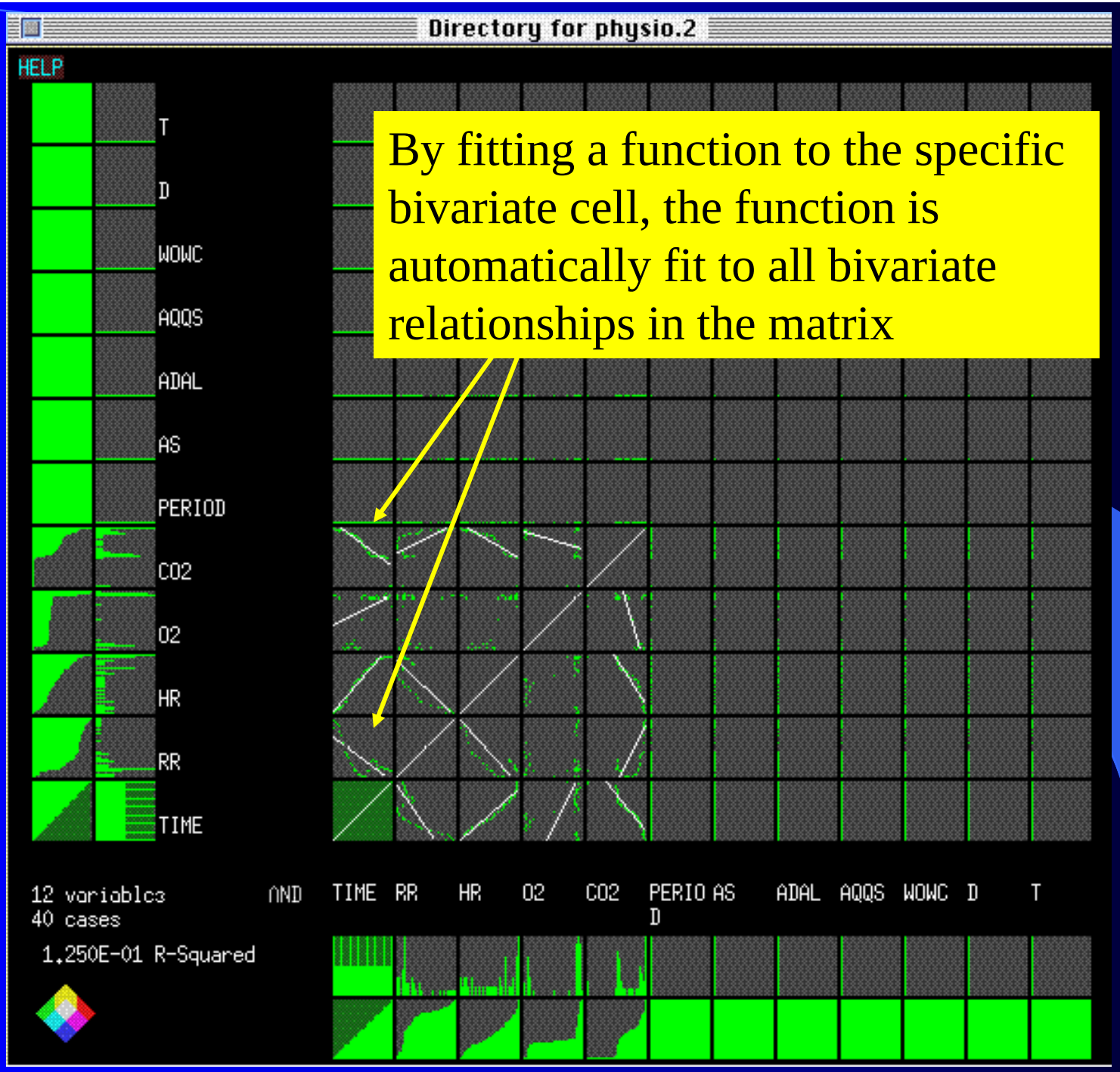

Pair-Wise physio.1 AS / TIME
HELP
+ AS
1
0
250
AS
1
0
210
AS / TIME
1
0
1
250
Cases
Correlation
Slope
250
-0,333
-0,169E-02
40
0
0
210
0
0
TIME
8
1
250
+ TIME
250
1
250
Reinvoking on the marked area subsets all the data again for this specific 40 second offset

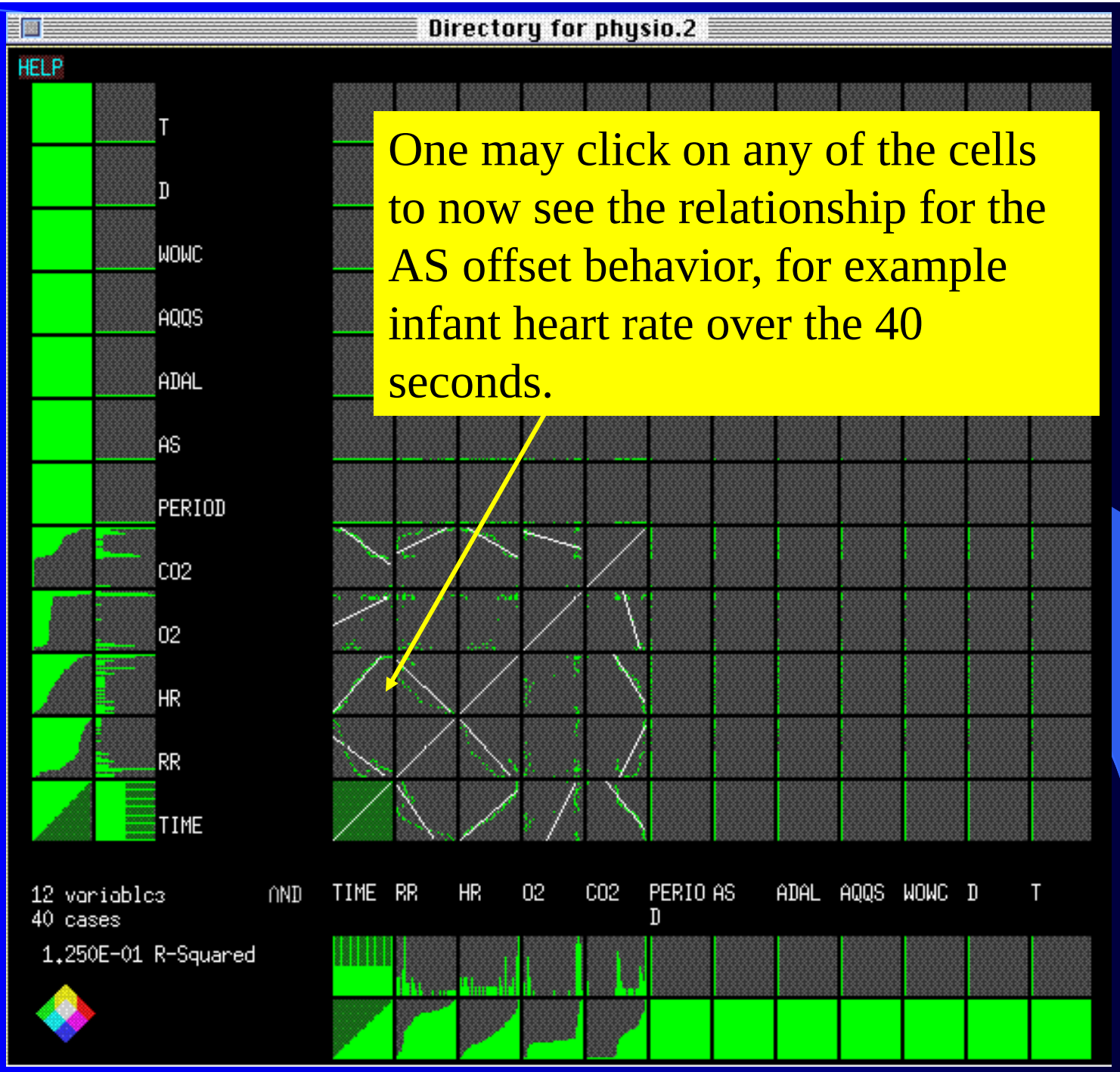

Directory for physio.2
HELP
T
D
WOWC
AQQS
ADAL
AS
PERIOD
CO2
O2
HR
RR
TIME
All data have now been subsetted for the specific 40 second offset period for AS behavior.
12 variables
40 cases
AND
TIME
RR
HR
O2
CO2
PERIO D
AS
ADAL
AQQS
WOWC
D
T


Directory for physio.2
HELP
T
D
WOWC
AQQS
ADAL
AS
PERIOD
CO2
O2
HR
RR
TIME
12 variables
40 cases
AND
TIME
RR
HR
O2
CO2
PERIO D
AS
ADAL
AQQS
WOWC
D
T
Now clicking on any of the bivariate cells will show the relationship relative to the AS behavior offset.


Pair-Wise physio.2 CO2 / TIME
HELP
+ CO2
51.5
0
40
CO2
51.5
0
8
CO2 / TIME
51.5
0
161
200
Cases Correlation Slope
40 -0.919 -1.024
40 -0.919 -1.024
TIME
2
161
200
+ TIME
40
161
200
Here one sees the relationship between CO2 and time during the AS behavioral offset.


Pair-Wise physio.2 CO2 / TIME
HELP
+ CO2
51.5
0
40
CO2
51.5
0
8
CO2 / TIME
51.5
0
161
200
Cases Correlation Slope
40 -0.919 -1.024
40 -0.919 -1.024
TIME
2
161
200
+ TIME
40
161
200
One may, on-the-fly, fit various functions to the data, in this case a linear function and obtain function parameters.


Directory for physio.2
HELP
T
D
WOWC
AQQS
ADAL
AS
PERIOD
CO2
O2
HR
RR
TIME
By fitting a function to the specific bivariate cell, the function is automatically fit to all bivariate relationships in the matrix
12 variables
40 cases
AND
TIME RR HR O2 CO2 PERIO AS ADAL AQQS WOWC D T
D
1.250E-01 R-Squared

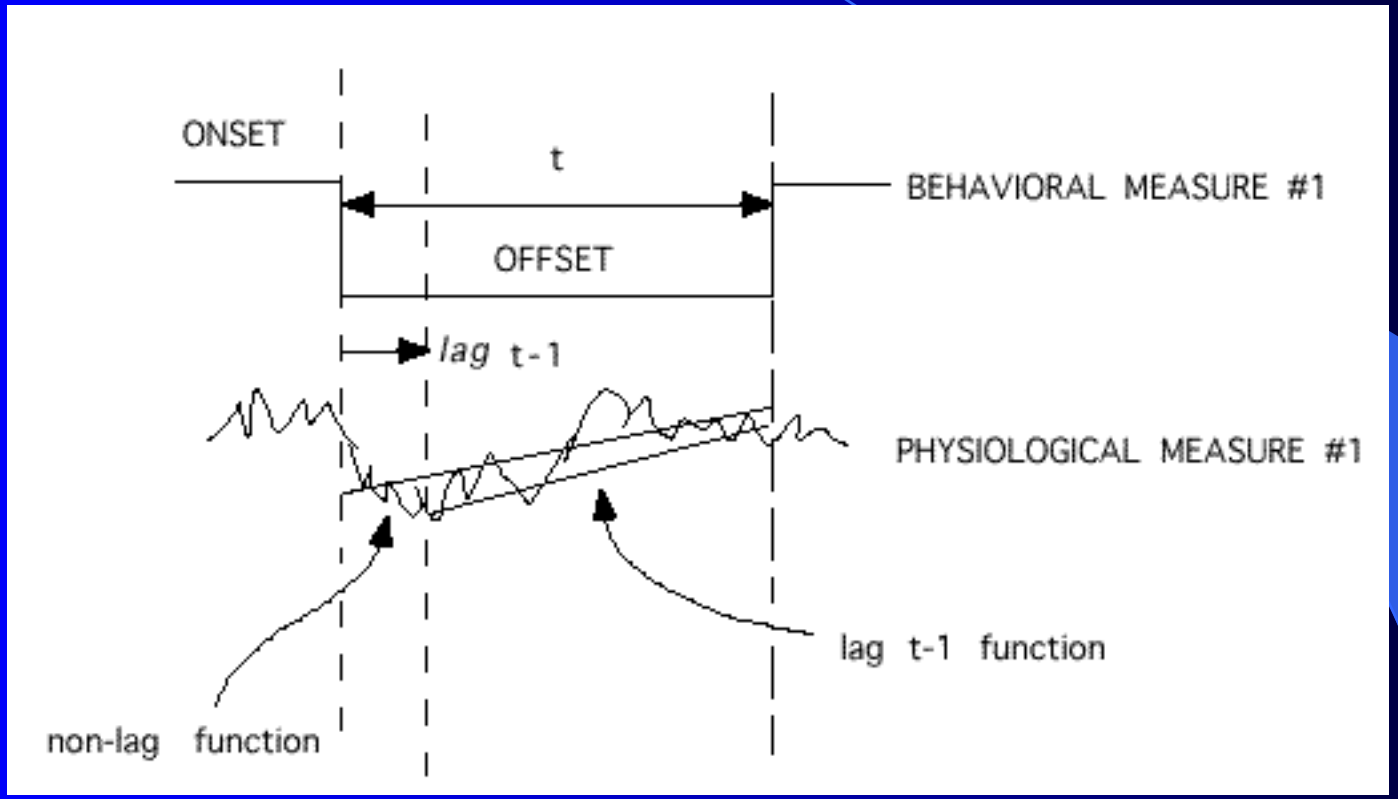

Directory for physio.2
HELP
T
D
WOWC
AQQS
ADAL
AS
PERIOD
CO2
O2
HR
RR
TIME
One may click on any of the cells to now see the relationship for the AS offset behavior, for example infant heart rate over the 40 seconds.
12 variables
40 cases
AND
TIME RR HR O2 CO2 PERIO D AS ADAL AQQS WOWC D T
1.250E-01 R-Squared

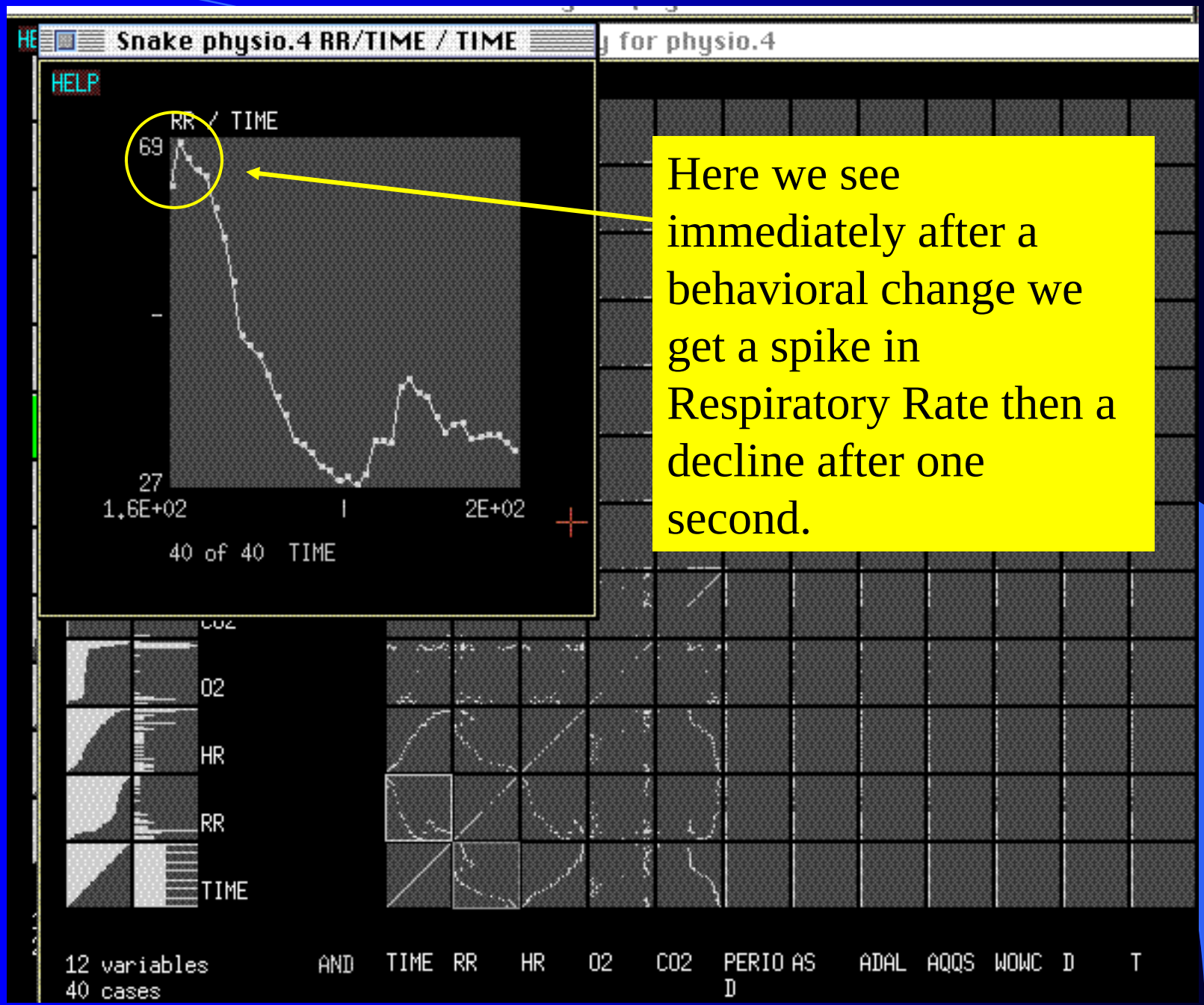

Pair-Wise physio.2 HR / TIME
HELP
+ HR
189
167
40
HR
189
167
6
HR / TIME
189
167
161
200
Cases
Correlation
Slope
40
0.981
0.623
40
0.981
0.623
TIME
2
161
200
+ TIME
40
161
200
Infant heart rate increases linearly over the 40 seconds

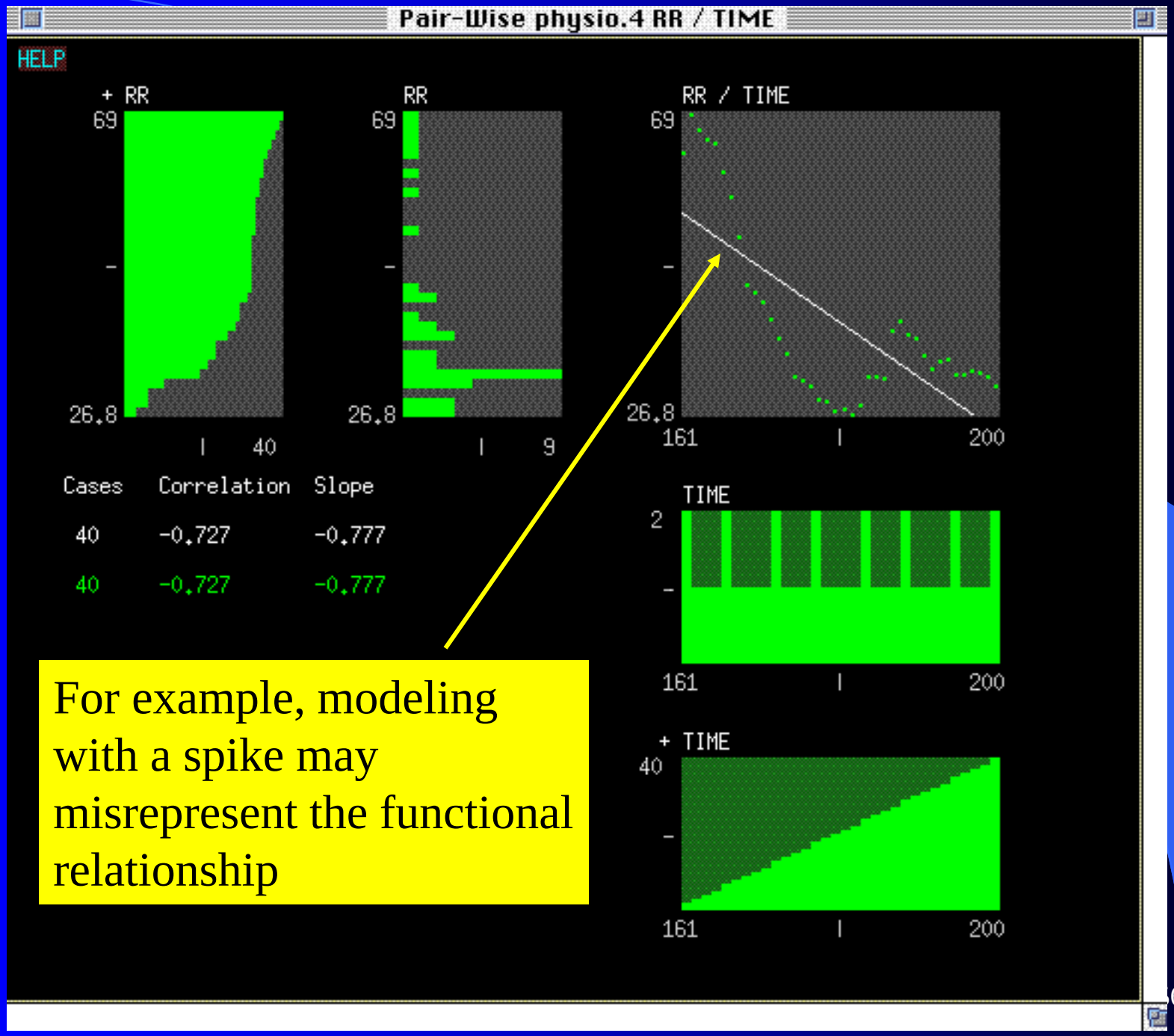
A Major Complicating Factor in Modeling Multiple Time-Series data is the Concept of Lag Functions.

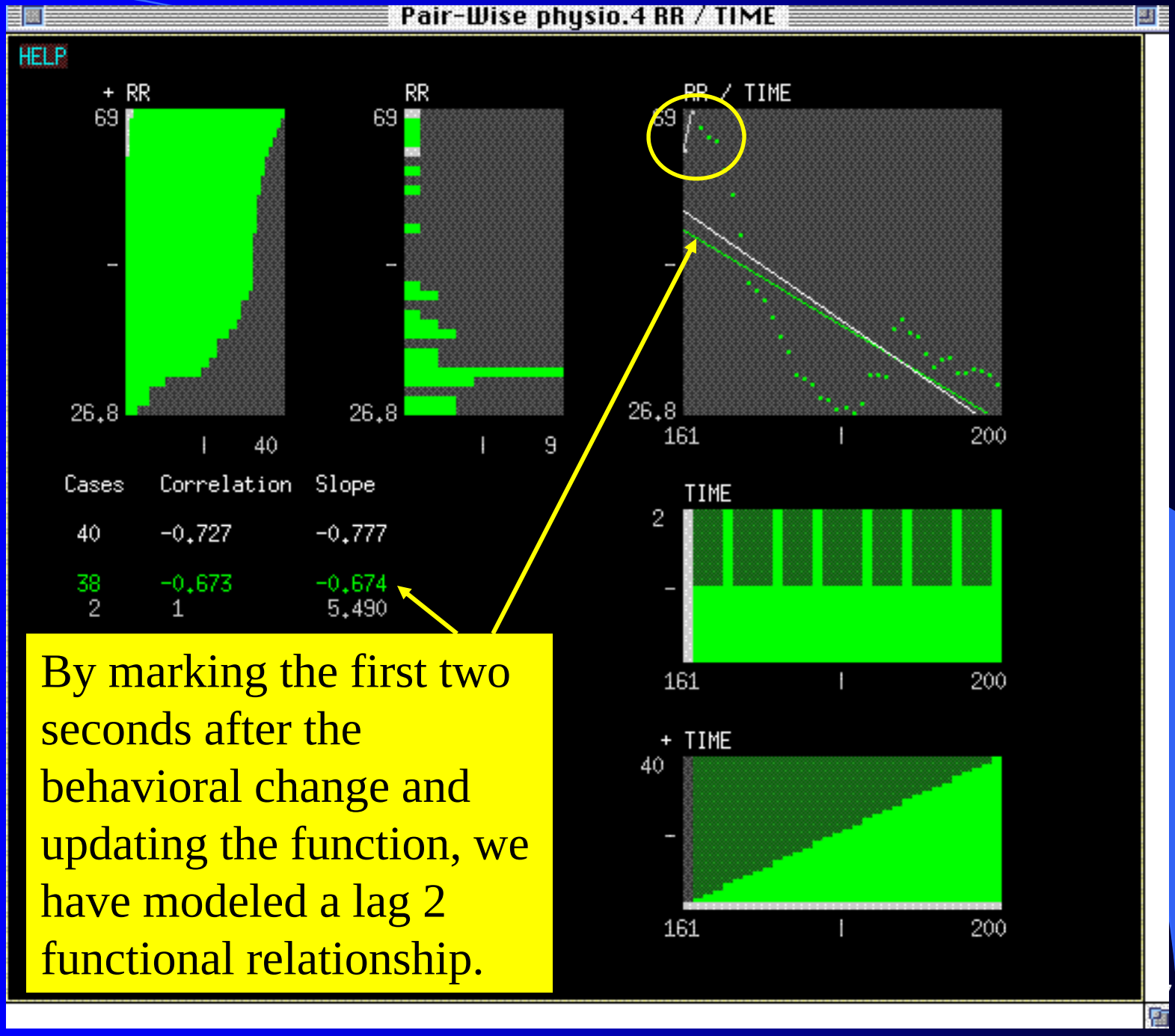
When do things changes?

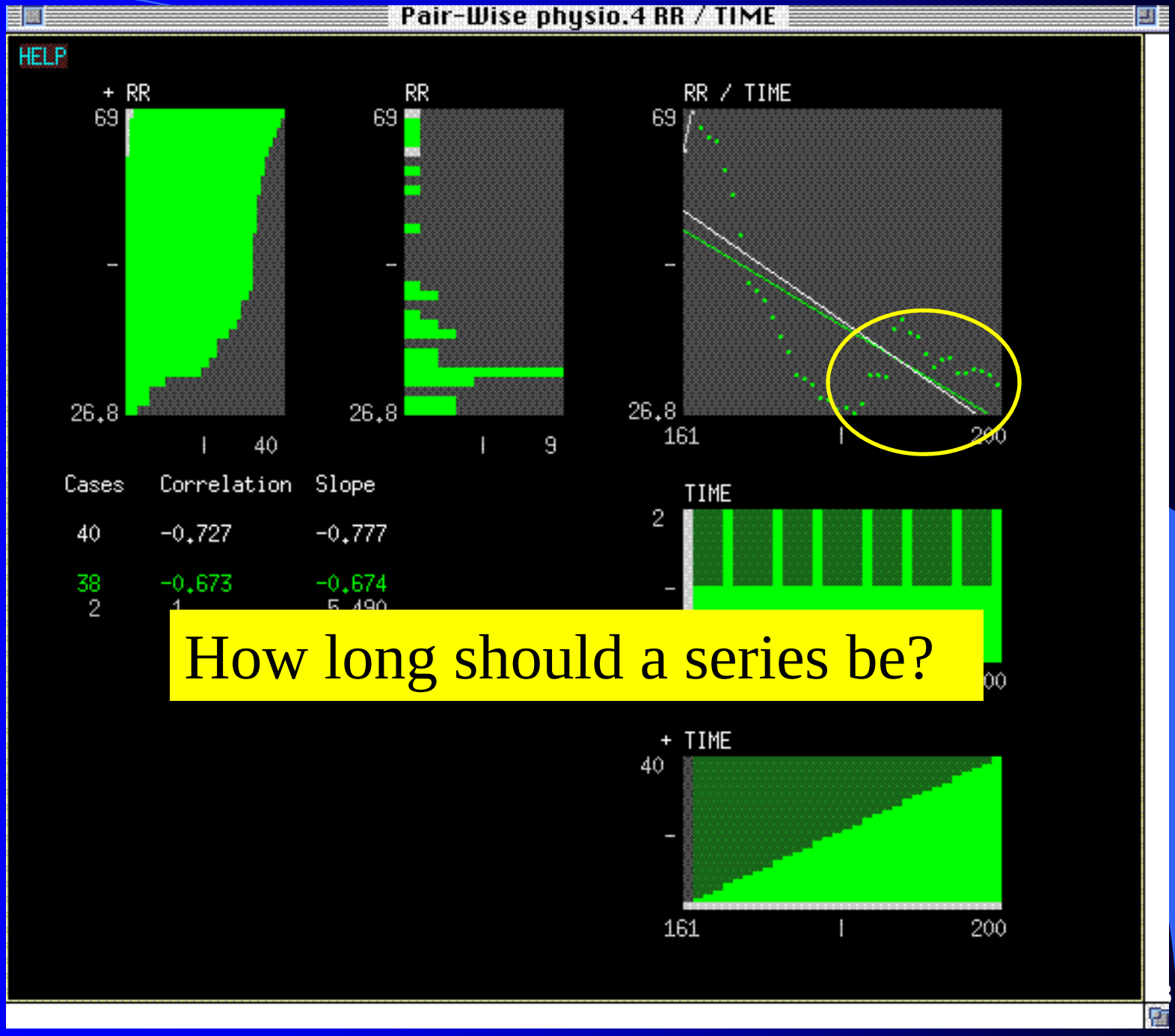
A physiological measure may not change immediately after a behavioral change, there may exist a lagged period of time prior to the change.

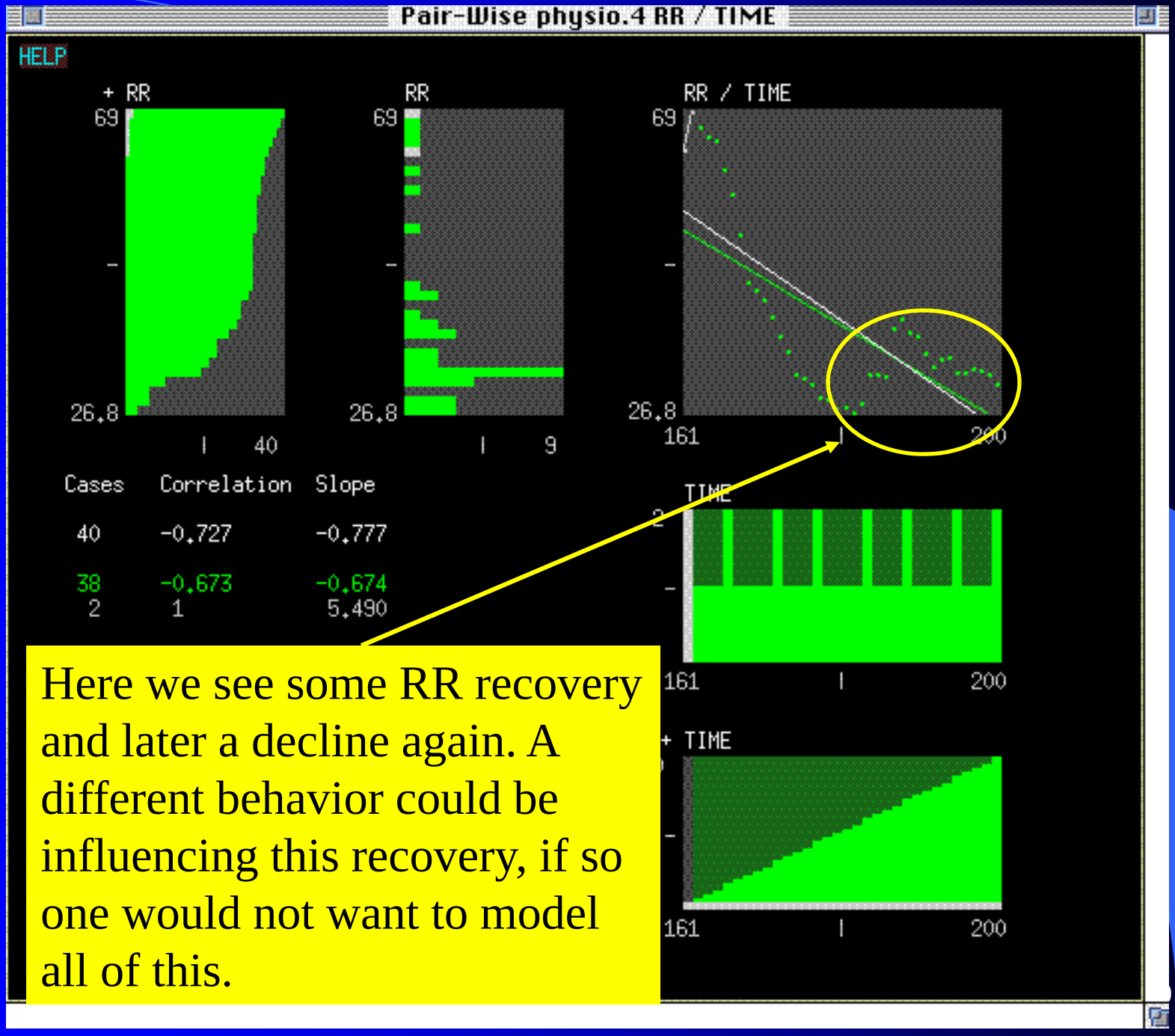


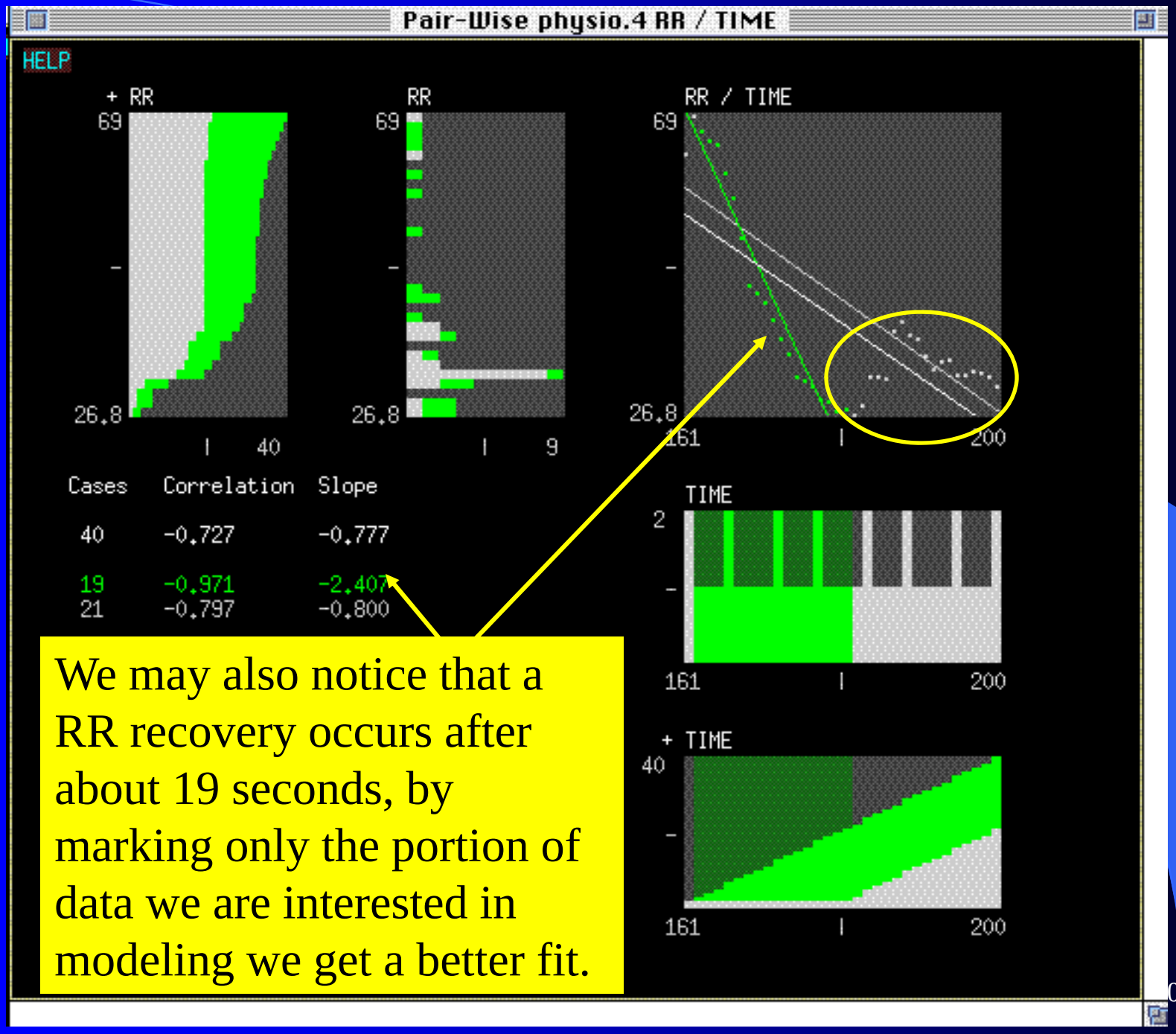

Snake physio.4 RR/TIME / TIME
HELP
RR / TIME
69
27
1.6E+02
2E+02
40 of 40 TIME
Here we see immediately after a behavioral change we get a spike in Respiratory Rate then a decline after one second.
O2
HR
RR
TIME
12 variables
40 cases
AND TIME RR HR O2 CO2 PERIOD AS ADAL AQQS WOWC D T


Pair-Wise physio.4 RR / TIME
HELP
+ RR
69
26.8
40
RR
69
26.8
9
RR / TIME
69
26.8
161
200
Cases
Correlation
Slope
40
-0.727
-0.777
40
-0.727
-0.777
TIME
2
161
200
+ TIME
40
161
200
For example, modeling with a spike may misrepresent the functional relationship

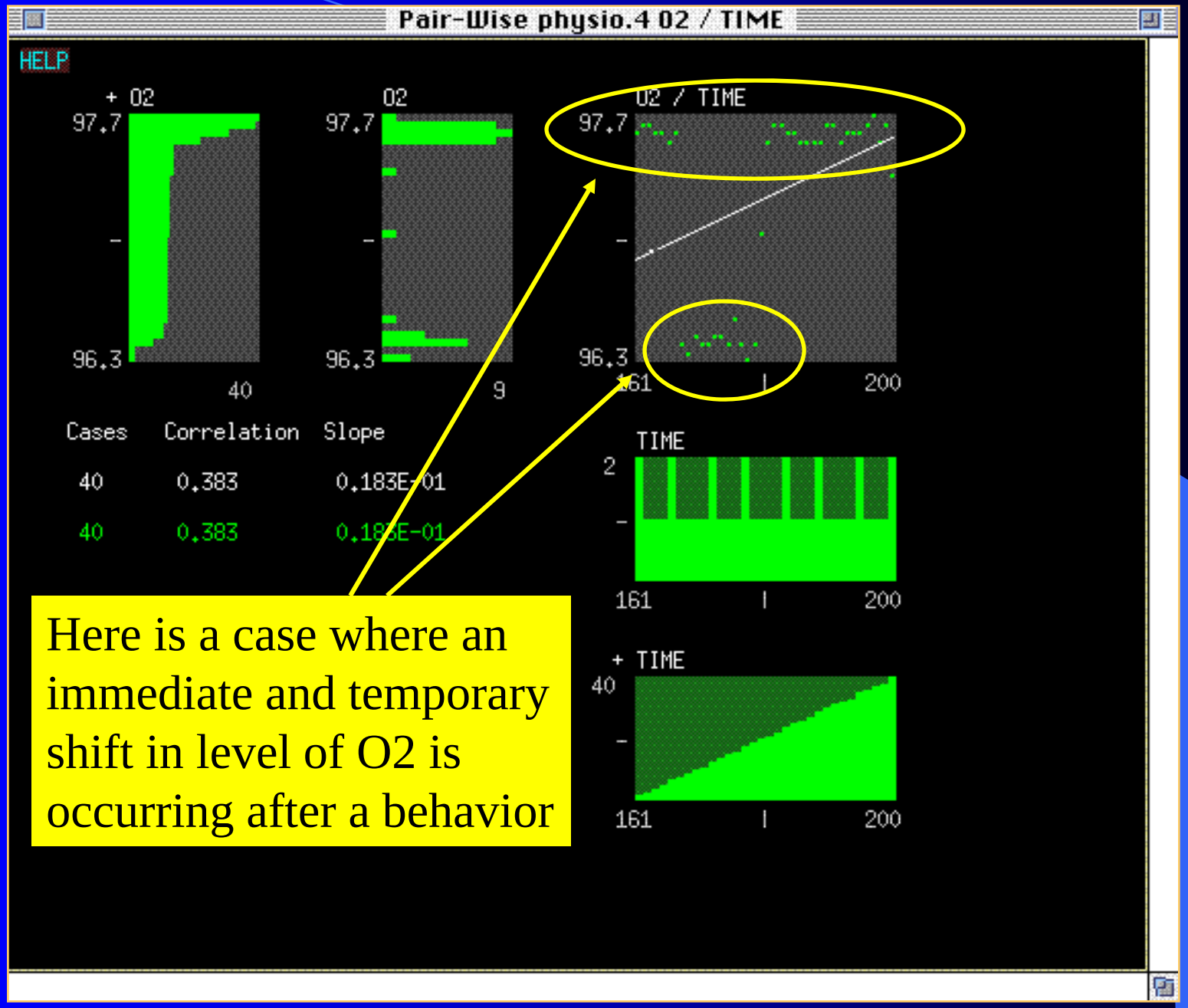

Pair-Wise physio.4 RR / TIME
HELP
+ RR
69
26.8
40
RR
69
26.8
9
RR / TIME
69
26.8
161
200
Cases Correlation Slope
40 -0.727 -0.777
38 -0.673 -0.674
2 1 5.490
TIME
2
161
200
+ TIME
40
161
200
By marking the first two seconds after the behavioral change and updating the function, we have modeled a lag 2 functional relationship.

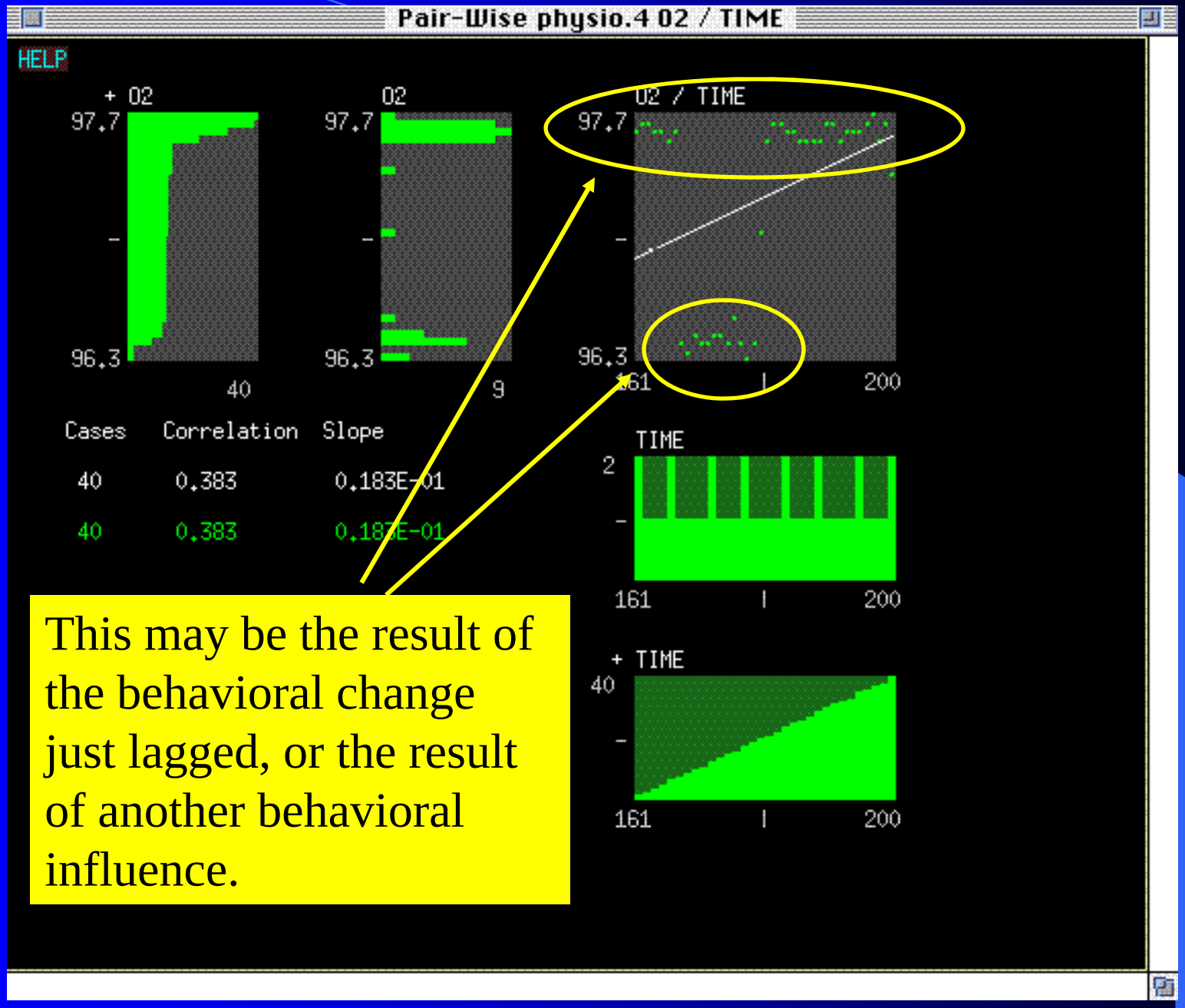

Pair-Wise physio.4 RR / TIME
HELP
+ RR
69
26.8
40
RR
69
26.8
9
RR / TIME
69
26.8
161
200
Cases
Correlation
Slope
40
-0.727
-0.777
38
-0.673
-0.674
2
TIME
2
+ TIME
40
161
200
How long should a series be?

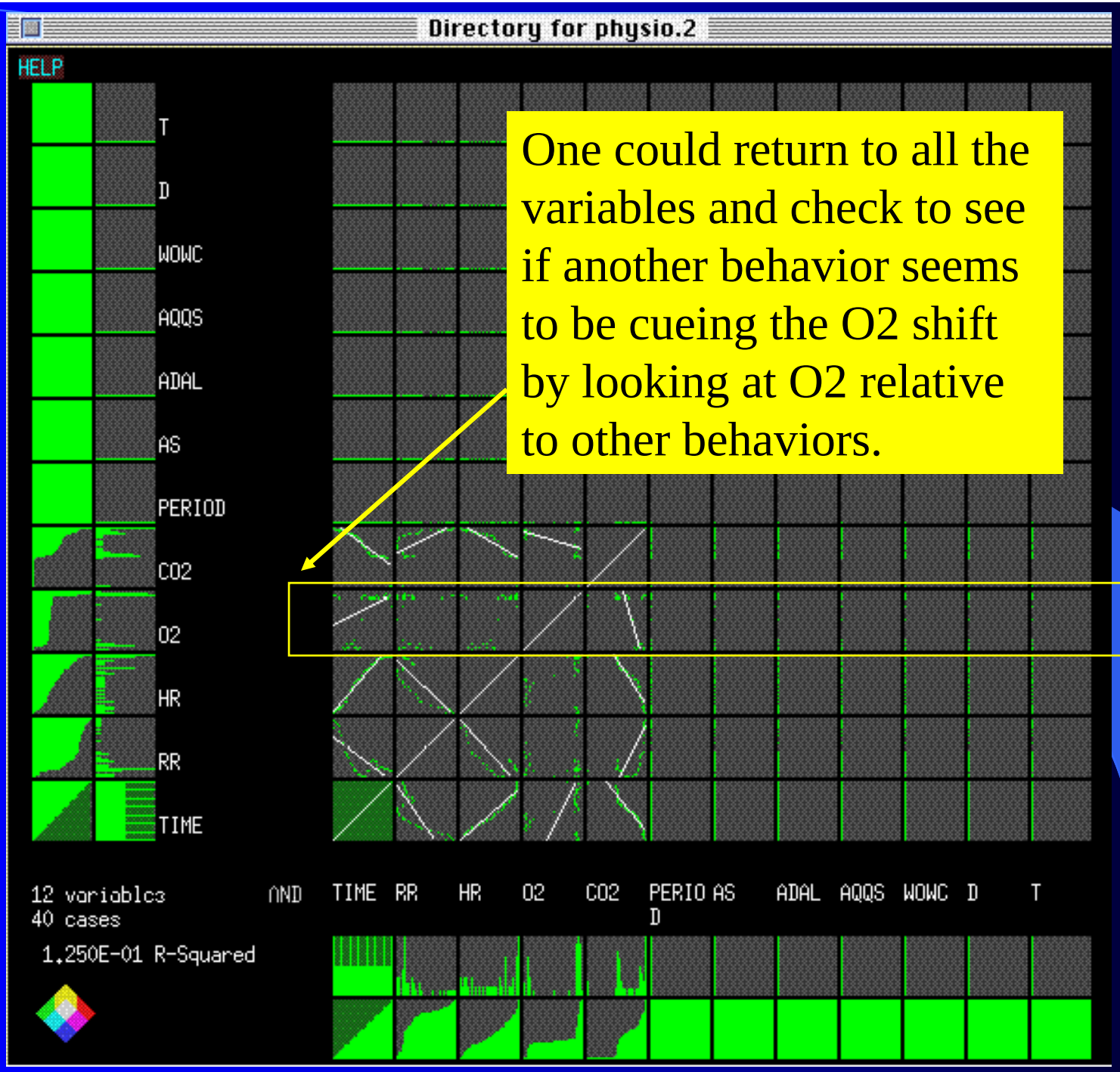

Pair-Wise physio.4 RR / TIME
HELP
+ RR
69
26.8
40
RR
69
26.8
9
RR / TIME
69
26.8
161
200
Cases Correlation Slope
40 -0.727 -0.777
38 -0.673 -0.674
2 1 5.490
TIME
161
200
+ TIME
161
200
Here we see some RR recovery and later a decline again. A different behavior could be influencing this recovery, if so one would not want to model all of this.

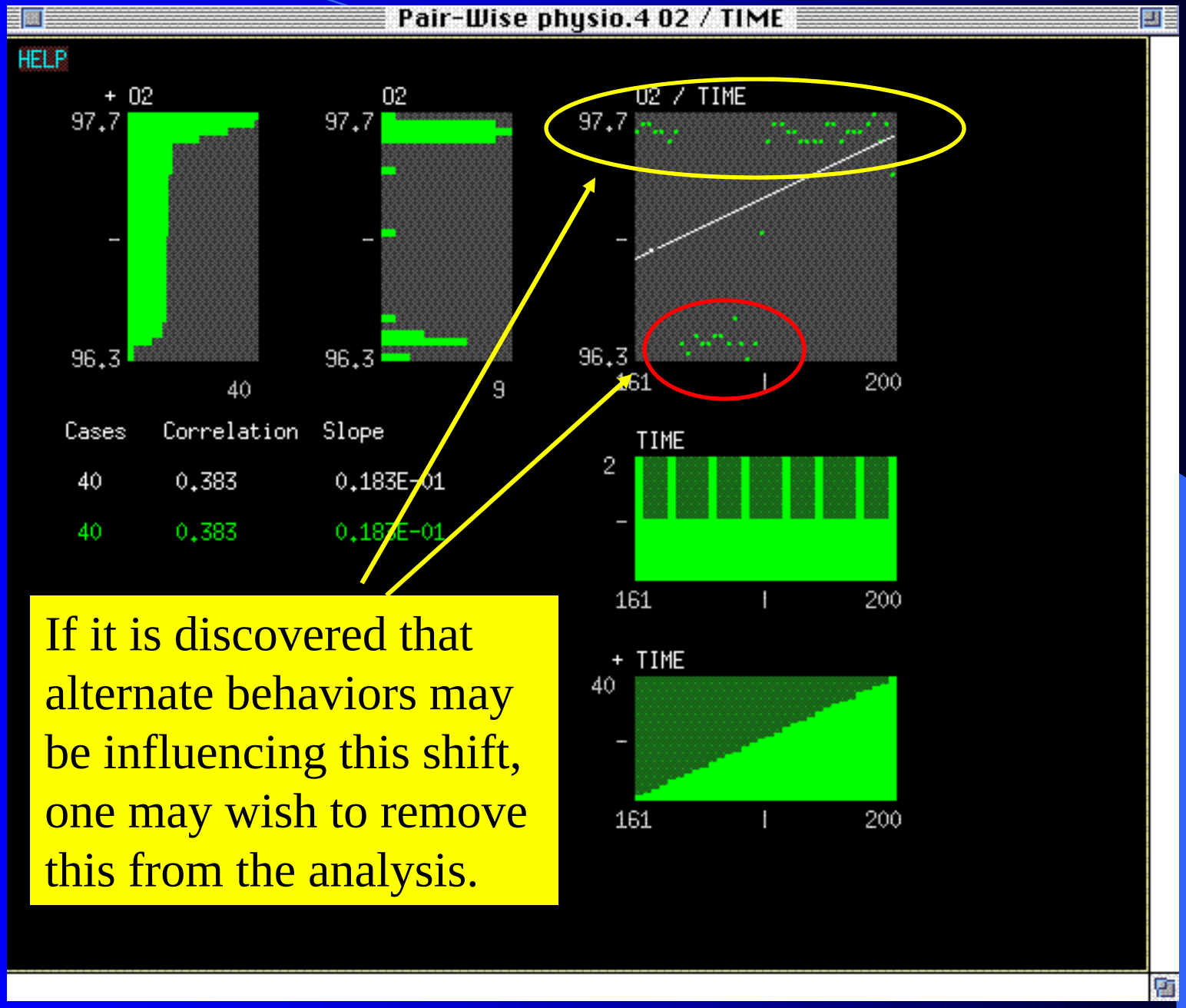

Pair-Wise physio.4 RR / TIME
HELP
+ RR
69
26.8
40
RR
69
26.8
9
RR / TIME
69
26.8
161
200
Cases Correlation Slope
40 -0.727 -0.777
19 -0.971 -2.407
21 -0.797 -0.800
TIME
2
161
200
+ TIME
40
161
200
We may also notice that a RR recovery occurs after about 19 seconds, by marking only the portion of data we are interested in modeling we get a better fit.

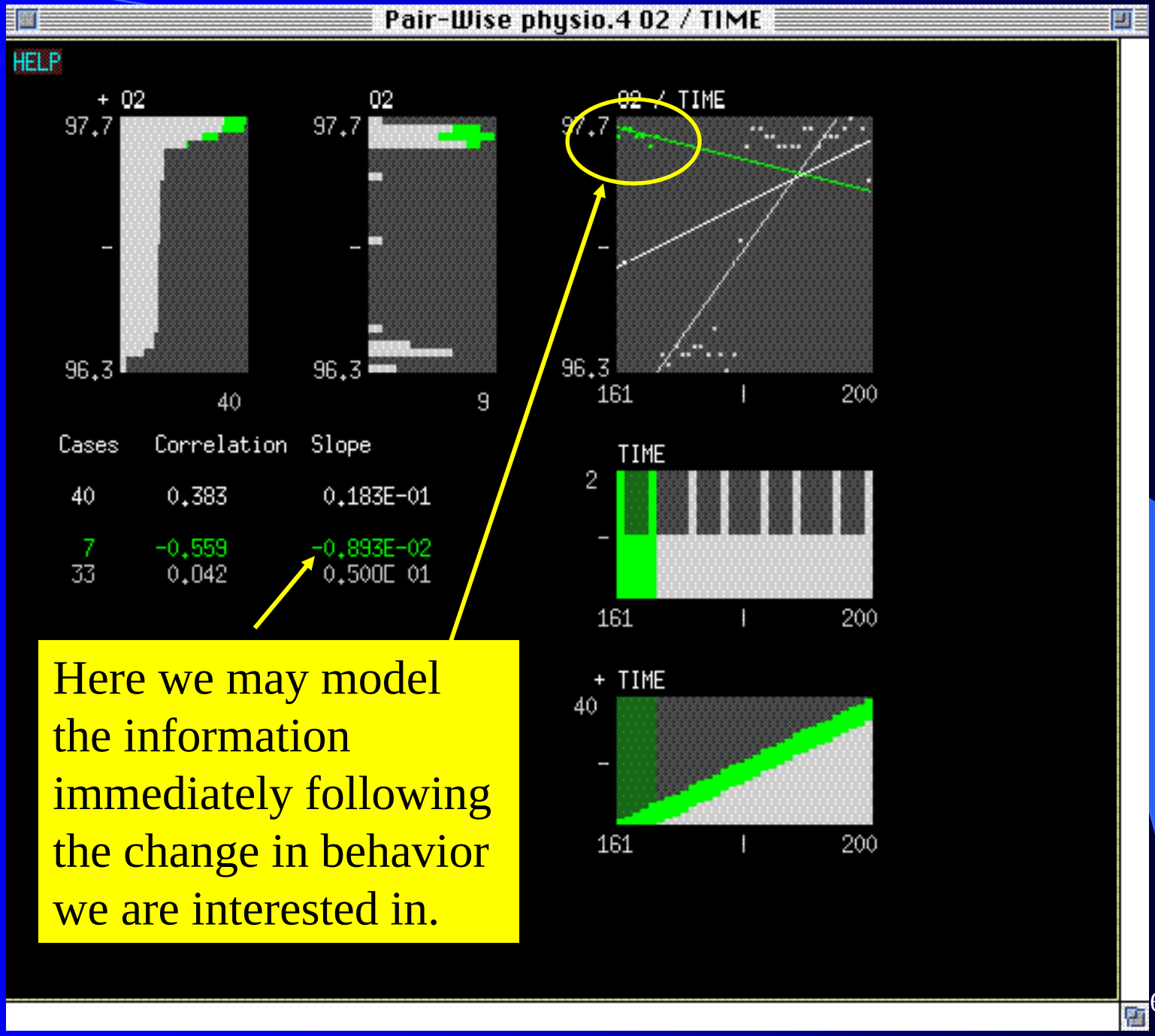
Working with Highly Variant Data

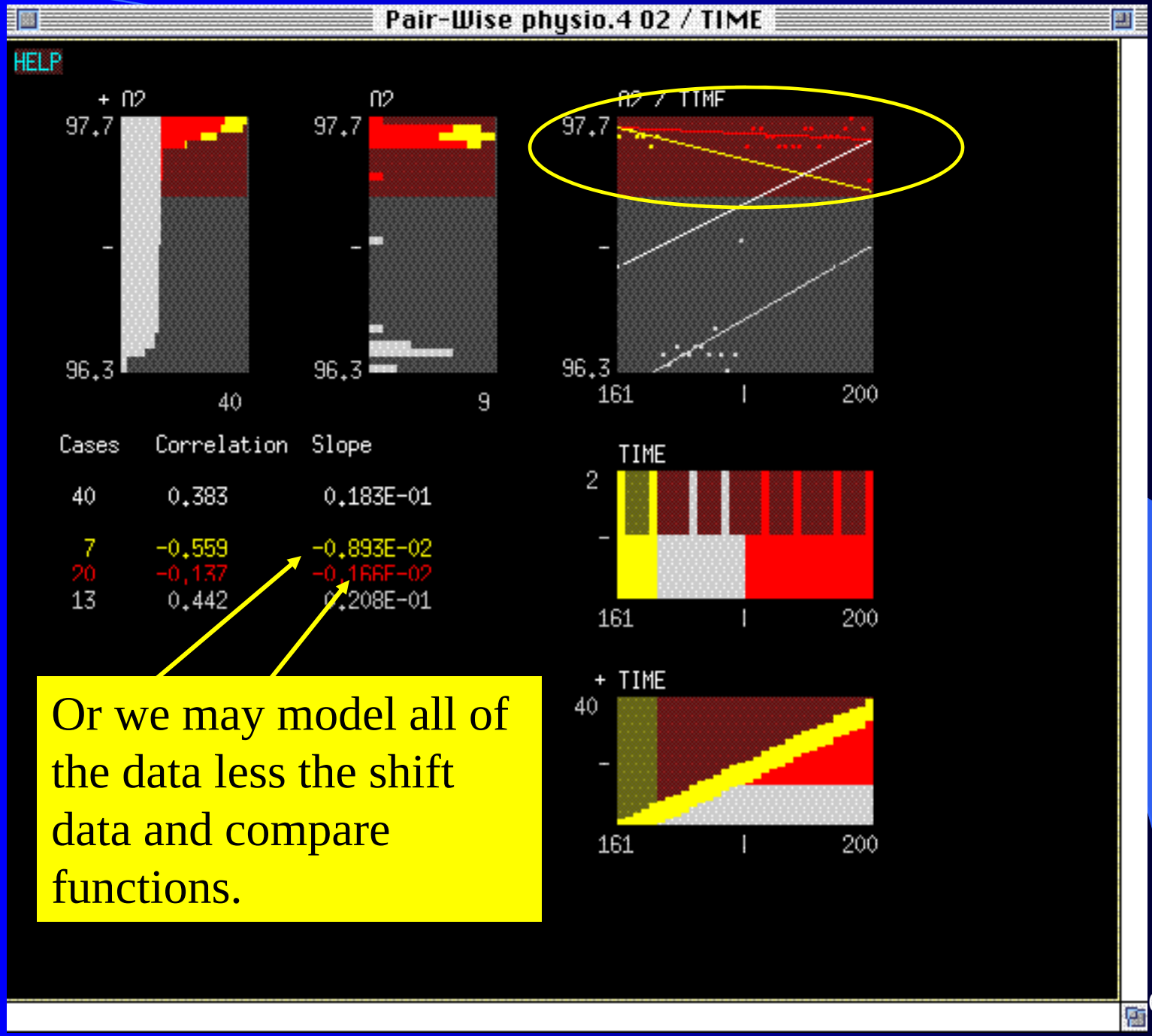

Pair-Wise physio.4 02 / TIME
HELP
+ 02
97.7
96.3
40
02
97.7
96.3
9
02 / TIME
97.7
96.3
161
200
Cases
Correlation
Slope
40
0.383
0.183E-01
40
0.383
0.183E-01
TIME
2
161
200
+ TIME
40
161
200
Here is a case where an immediate and temporary shift in level of O2 is occurring after a behavior


Pair-Wise physio.4 02 / TIME
HELP
+ 02
97.7
96.3
40
02
97.7
96.3
9
02 / TIME
97.7
96.3
161
200
Cases
Correlation
Slope
40
0.383
0.183E-01
40
0.383
0.187E-01
TIME
2
161
200
+ TIME
40
161
200
This may be the result of the behavioral change just lagged, or the result of another behavioral influence.


Directory for physio.2
HELP
T
D
WOWC
AQQS
ADAL
AS
PERIOD
CO2
O2
HR
RR
TIME
One could return to all the variables and check to see if another behavior seems to be cueing the O2 shift by looking at O2 relative to other behaviors.
12 variables
40 cases
AND
TIME RR HR O2 CO2 PERIO AS ADAL AQQS WOWC D T
D
1.250E-01 R-Squared


Pair-Wise physio.4 02 / TIME
HELP
+ 02
97.7
96.3
40
02
97.7
96.3
9
02 / TIME
97.7
96.3
161
200
Cases
Correlation
Slope
40
0.383
0.183E-01
40
0.383
0.187E-01
TIME
2
161
200
+ TIME
40
161
200
If it is discovered that alternate behaviors may be influencing this shift, one may wish to remove this from the analysis.


Pair-Wise physio.4 02 / TIME
HELP
+ 02
97.7
96.3
40
02
97.7
96.3
9
02 / TIME
97.7
96.3
161
200
Cases
Correlation
Slope
40
0.383
0.183E-01
7
-0.559
-0.893E-02
33
0.042
0.500E 01
TIME
2
161
200
+ TIME
40
161
200
Here we may model the information immediately following the change in behavior we are interested in.


Pair-Wise physio.4 02 / TIME
HELP
+ 02
97.7
96.3
40
02
97.7
96.3
9
02 / TIME
97.7
96.3
161
200
Cases
Correlation
Slope
40
0.383
0.183E-01
7
-0.559
-0.893E-02
20
-0.137
-0.168E-02
13
0.442
0.208E-01
TIME
2
161
200
+ TIME
40
161
200
Or we may model all of the data less the shift data and compare functions.

Using this approach also allows one to create the appropriate sub-setted hierarchical dataset need for the analysis

Conclusion

Attempting to model such complex multivariate nested time series should not be done without some prior exploration. While this is somewhat time consuming, it provides for better success in fitting mathematical models and helping understand the functional relationships.

Current Investigations using this Method

- **S. Thoyre (UNC) and R.L. Brown (UW).**
- **This exploratory analysis in conjunction with hierarchical growth modeling is being used to model differential oxygen recovery curves in premature infants after feeding episodes.**

Current Investigations using this Method

- **D. Lanuza (UW), C. Lefaiver (Loyola) and R. L. Brown (UW)**
- This approach is also being used to study and model nocturnal blood pressure decline in pre and post-transplant patients.

Recent Publications Based on Dynamic Multidimensional Graphics

Thoyre, S., and Brown, R. L. (2004). Factors contributing to preterm infant engagement during bottle-feeding. Nursing Research, 53(5), 304-313.