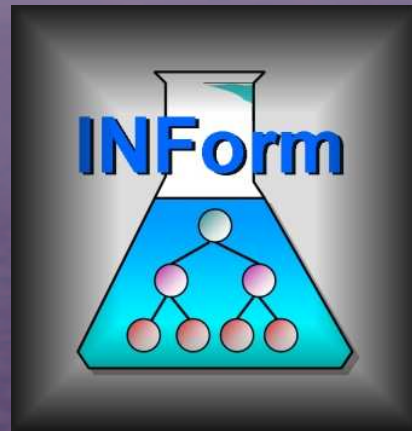


INForm



Better Products **Faster** -
Models and Optimization for
Product Formulation

What is INForm?

- A Windows-based software package developed by Intelligensys
 - Designed to be used by product formulators themselves
- Based on artificial intelligence and evolutionary computing techniques
 - To 'learn' cause-and-effect relationships within experimental data, automatically

Why? Worldwide Competition Requires Better Products... *Faster*

- improved product properties
- consistent quality
- more efficient processing
- lower cost
- shorter time to market

INForm can help you...

- discover better product formulations to meet customer needs, increasing your responsiveness
- decrease development costs
- reduce wasted time and materials
- reduce time to market for new or improved products, to enhance your competitiveness and profitability
- Using proven state-of-the art computational methods

Who uses INForm?

- Companies like AstraZeneca, Pfizer, Dow Chemical, Cabot Microelectronics, Armstrong, International Paints, Lucite and many others...
- Academic groups in Europe, America and Asia

How does INForm work?

- You collect experimental data by varying the 'recipe' (ingredients and process conditions) and measuring end-use properties
- Then import this data into INForm
- INForm will develop cause-and-effect models relating inputs and outputs
- You use the models for prediction and optimization

What's inside INForm?

- INForm uses neural networks and Gene Expression Programming to develop cause-and-effect models
 - Works well even for non-linear and complex situations
- INForm uses genetic algorithms for optimization
 - with fuzzy logic to help you to define your objectives intuitively

What you'll see here

- This presentation will show you some of the key aspects of INForm, illustrated using a data set for an immediate-release pharmaceutical tablet formulation
- Because INForm works on your own data, though, it can be applied much more widely to many formulations and processing situations. See the on-line application notes for some examples.

Collecting Data – the first step

- Save your data in a spreadsheet or tab-delimited file
- Each row corresponds to a separate experiment or 'recipe'
- First row contains the 'field names' describing your inputs and outputs

Data

- The following slide shows part of a data set for a tablet formulation, used in our example
- Here, there are 5 inputs
 - Diluent, Diluent %, PVP %, Binder addition and Granulation equipment
- And 4 tablet properties
 - Hardness, friability, thickness and disintegration time

Part of a typical data set

Diluent	Diluent%	PVP%	Binder-addn	Gran-equip	Hardness	Friability	Thickness	Disinteg-time
Lactose	47.5	2	dry	Fluidized Bed	5.56	2.89	3.35	550
Lactose	46.5	3	dry	Fluidized Bed	5.01	2.92	3.36	633
Lactose	45.5	4	dry	Fluidized Bed	3.84	3.72	3.3	827
Lactose	44.5	5	dry	Fluidized Bed	4.56	1.79	3.3	651
Lactose	47.5	2	wet	Fluidized Bed	4.33	3.9	3.256	528
Lactose	46.5	3	wet	Fluidized Bed	4.18	3.66	3.281	687
Lactose	45.5	4	wet	Fluidized Bed	7.7	0.47	3.314	867
Lactose	44.5	5	wet	Fluidized Bed	8.56	0.38	3.4	1040
Ditab	47.5	2	dry	Fluidized Bed	5.56	2.89	3.35	550
Ditab	46.5	3	dry	Fluidized Bed	5.01	2.92	3.36	633
Ditab	45.5	4	dry	Fluidized Bed	3.84	3.72	3.3	827
Ditab	44.5	5	dry	Fluidized Bed	4.56	1.79	3.3	651
Ditab	47.5	2	wet	Fluidized Bed	4.33	3.9	3.256	528
Ditab	46.5	3	wet	Fluidized Bed	4.18	3.66	3.281	687
Ditab	45.5	4	wet	Fluidized Bed	7.7	0.47	3.314	867
Ditab	44.5	5	wet	Fluidized Bed	8.56	0.38	3.4	1040
Lactose	47.5	2	dry	High Shear Mixer	9.41	0.22	3.342	442
Lactose	46.5	3	dry	High Shear Mixer	10.78	0.15	3.262	626
Lactose	45.5	4	dry	High Shear Mixer	10.5	0.1	3.358	713
Lactose	44.5	5	dry	High Shear Mixer	10.08	0.08	3.359	750

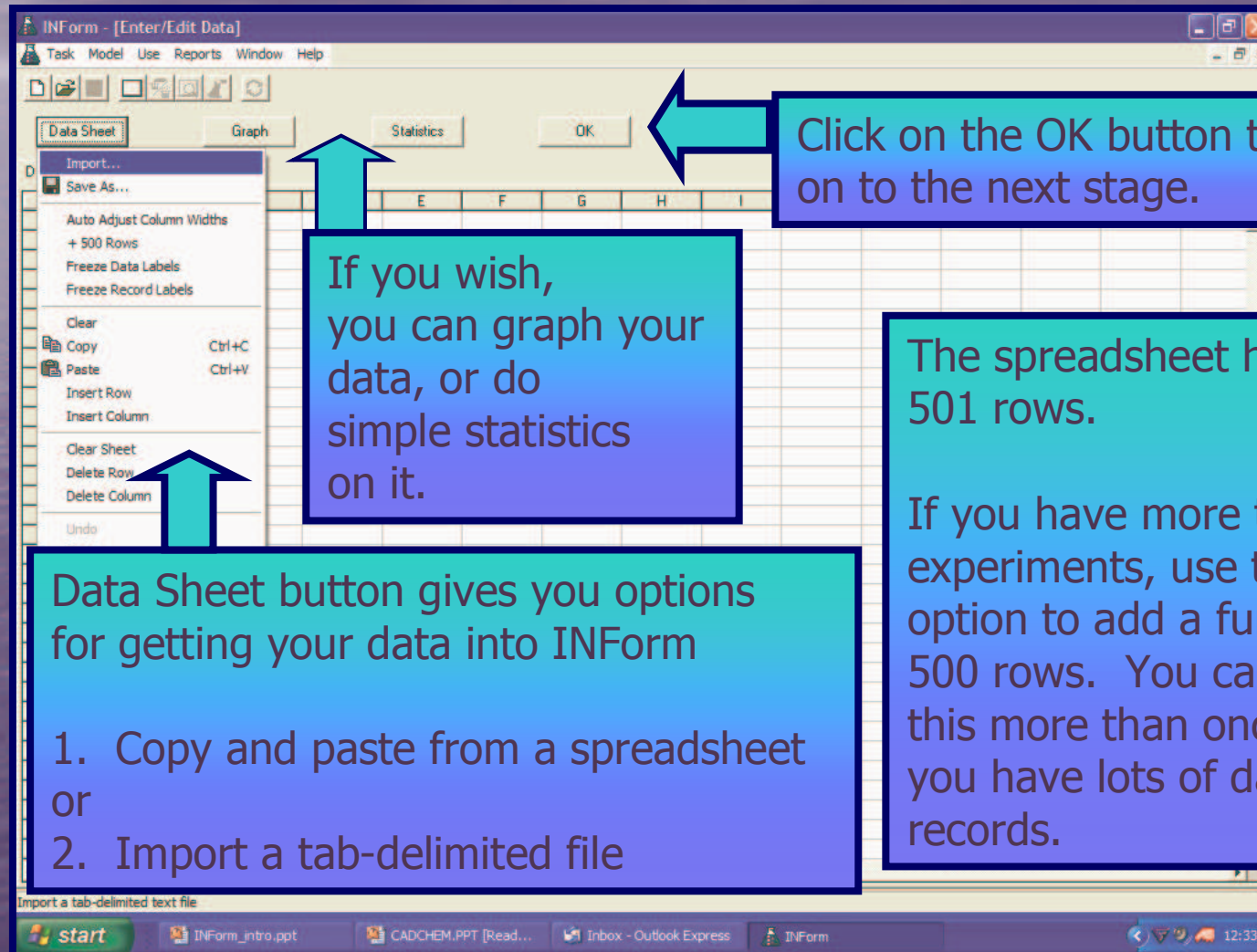
Each row describes a separate formulation. Ingredient names, process conditions and properties are given in the first row.

Typically you need at least 2-3 times as many experiments as you have inputs, to get a good model.

Loading Data

- When you launch INForm, you'll see a spreadsheet
- Just copy-and-paste your own data...
- You can have up to 150 inputs/outputs, and as many experiments as you want. (The initial spreadsheet is set up for 500, but you can add more rows to the sheet.)

First, enter your data



Click on the OK button to move on to the next stage.

If you wish, you can graph your data, or do simple statistics on it.

Data Sheet button gives you options for getting your data into INForm

1. Copy and paste from a spreadsheet or
2. Import a tab-delimited file

The spreadsheet has 501 rows.

If you have more than 500 experiments, use the +500 option to add a further 500 rows. You can do this more than once if you have lots of data records.

Then, set inputs and outputs

The screenshot shows the INForm software interface with a table of field types. The table has columns for Field Name, Field Type, Units, Min, Max, Global Min, and Global Max. The 'Field Type' column is currently open, showing a list of options: Ingredient, Not Used, Processing Condition, and Property. A red box highlights the 'Quick Select' button in the bottom left corner of the interface.

	Field Name	Field Type	Units	Min	Max	Global Min	Global Max
1	Diluent	Ingredient		0.0000	1.0000		
2	Diluent%	Not Used		44.5000	47.5000		
3	PVP%	Ingredient		2.0000	5.0000		
4	Binder-addn	Processing Condition		0.0000	1.0000		
5	Gran-equip	Property		0.0000	1.0000		
6	Hardness	Not Used		3.8400	13.0000	3.8400	13.0000
7	Friability	Not Used					
8	Thickness	Not Used					
9	Disinteg-tir	Not Used					

Quick Select Previous Next Help Task Name: C:\Program Files\Intelligensy Browse

Set each variable as an Ingredient, Processing Condition or Property.

The Quick Select feature lets you pick blocks of ingredients, processing Conditions and properties, making it quick to set up all of the fields.

You can also get these options by right-clicking with the mouse anywhere over the screen, to get a small pop-up menu.

Setting inputs and outputs

The screenshot shows the INForm software interface with a table of field settings. The table has columns for Field Name, Field Type, Units, Min, Max, Global Min, and Global Max. The fields are numbered 1 through 9. The Field Type column contains 'Ingredient' for fields 1-5 and 'Property' for fields 6-9. The Units column is empty for all fields. The Min and Max columns contain numerical values for each field. The Global Min and Global Max columns also contain numerical values for each field.

	Field Name	Field Type	Units	Min	Max	Global Min	Global Max
1	Diluent	Ingredient		0.0000	1.0000	0.0000	1.0000
2	Diluent%	Ingredient		44.5000	47.5000	44.5000	47.5000
3	PVP%	Ingredient		2.0000	5.0000	2.0000	5.0000
4	Binder-addn	Ingredient		0.0000	1.0000	0.0000	1.0000
5	Gran-equip	Ingredient		0.0000	1.0000	0.0000	1.0000
6	Hardness	Property		3.8400	13.0000		
7	Friability	Property		0.0800	3.9000		
8	Thickness	Property		2.8120	3.4000		
9	Disinteg-time	Property		161.0000	1520.0000		

At the bottom of the window, there are buttons for 'Quick Select', 'Previous', 'Next', and 'Help'. The 'Task Name' field is set to 'C:\Program Files\Intelligensy' and there is a 'Browse' button next to it.

When inputs (ingredients and processing conditions) and outputs (properties) are set, the screen looks like this...

Click on **Next** to move on to Data Analysis.

Data Analysis

The screenshot shows the INForm software interface. At the top, there is a menu bar with 'Task', 'Model', 'Use', 'Reports', 'Window', and 'Help'. Below the menu bar is a toolbar with icons for file operations and analysis. A row of buttons includes 'Data Sheet', 'Graph', 'Statistics', 'Analyze', 'Previous', 'Next', and 'Help'. Below these buttons are two tabs: 'Complete Data' and 'Missing Data'. The main area displays a data table with columns A through H. An arrow points from a text box to the 'Graph' button.

Data points are split into 'complete' and 'missing data' sets

	A	B	C	D	E	F	G	H
1		Diluent	Diluent%	PVP%	Binder-addn	Gran-equip	Hardness	Friability
2	1	0	47.5	2	0	0	5.56	2.89
3	2	0	46.5	3	0	0	5.01	2.92
4	3	0	45.5	4	0	0	3.84	3.72
5	4	0	44.5	5	0	0	4.56	1.79
6	5	0	47.5	2	1	0	4.33	3.9
7	6	0	46.5	3	1	0	4.18	3.66
8	7	0	45.5	4	1	0	7.7	0.47
9	8	0	44.5	5	1	0	8.56	0.38
10	9	1	47.5	2	0	0	7.58	0.57
11	10	1	46.5	3	0	0	6.64	1.1
12	11	1	45.5	4	0	0	6.4	0.87
13	12	1	44.5	5	0	0	6.34	3.87
14	13	1	47.5	2	1	0	8.3	0.42
15	14	1	46.5	3	1	0	9.4	0.3
16	15	1	45.5	4	1	0	7.48	0.63
17	16	1	44.5	5	1	0	7.44	0.49
18	17	0	47.5	2	0	1	9.41	0.22
19	18	0	46.5	3	0	1	10.78	0.15
20	19	0	45.5	4	0	1	10.5	0.1

Data analysis allows:

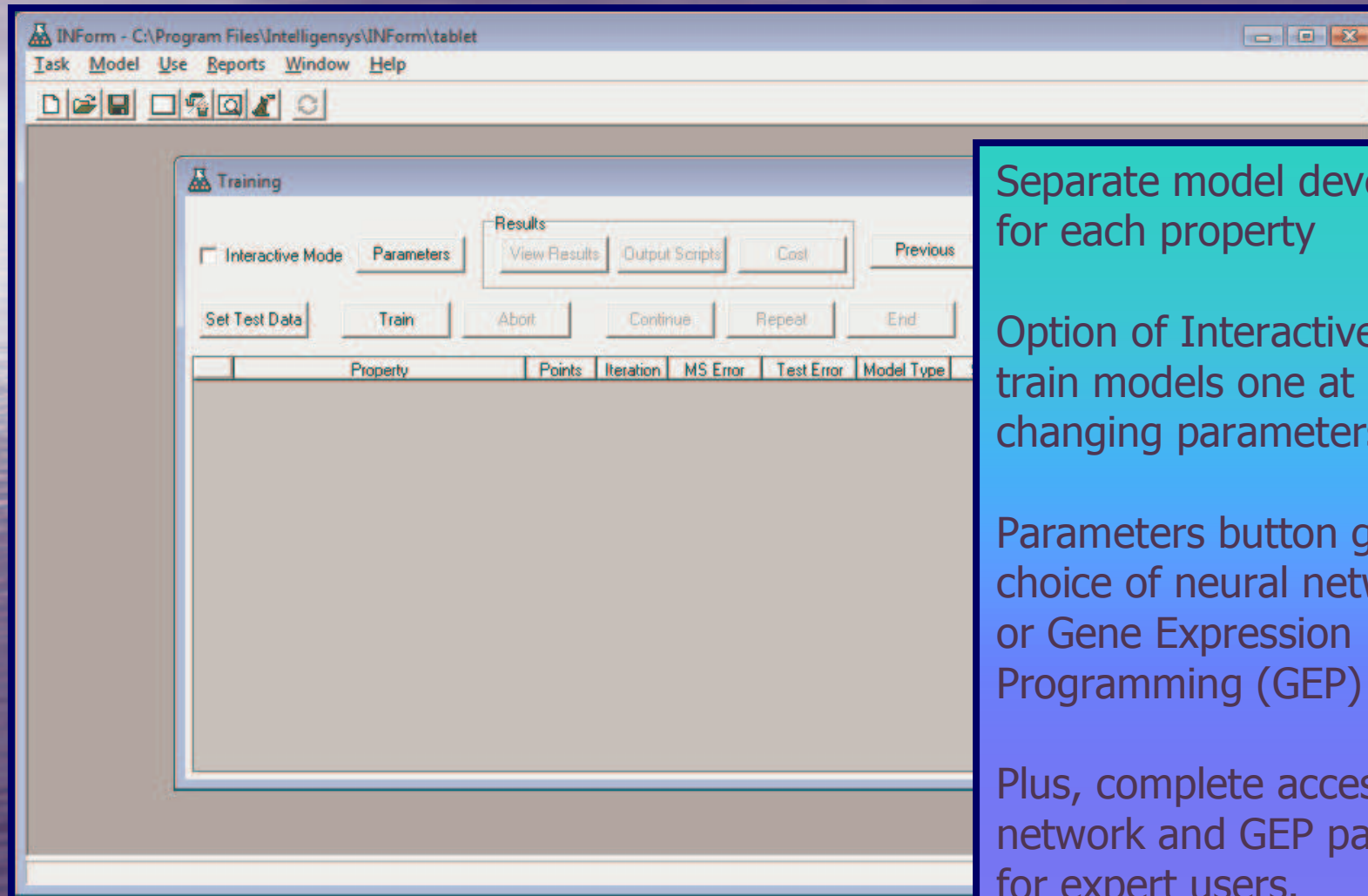
- Graphical display of data
- Statistical analysis
- Examination for outliers with **Analyze** button

Click on **Next** to move on to Training

What is 'Training'?

- Defined as the process of building a model that connects your inputs to outputs
 - Given specific inputs, the outputs are predicted in line with experimental findings
- INForm's training gives you the choice of neural networks or Gene Expression Programming to develop your models
 - 'learns' relationships from data provided by you, the user

The Training screen



Separate model developed for each property

Option of Interactive Mode to train models one at a time, changing parameters if desired

Parameters button gives choice of neural networks or Gene Expression Programming (GEP)

Plus, complete access to neural network and GEP parameters for expert users.

Validation

- Models 'learn' from data
- Risk of 'over-training' especially for neural networks, so they might learn noise as well as real relationships
- Avoid this by saving some 'Test Data'
 - Not used for training
 - Predict properties for these points, compare with known measured properties, to assess model's validity

Selecting Test Data

The screenshot shows the INForm software interface. The main window is titled "INForm - C:\Program Files\Intelligensys\INForm\NewData - [Set Test Data]". The menu bar includes "Task", "Model", "Use", "Reports", "Window", and "Help". The toolbar contains icons for file operations and a "Data Sheet" button. Below the toolbar are buttons for "Options", "OK", "Cancel", and "Help". The "Options" button is highlighted with a blue arrow pointing to the "Test Data Options" dialog box.

The "Test Data Options" dialog box has the following options:

- Test Data
 - None
 - Manually selected
 - Random selection
 - Smart selection
 - Import test data
- Random Percentage: 10 % of Total Patterns
- External File: Import...
- Buttons: OK, Cancel

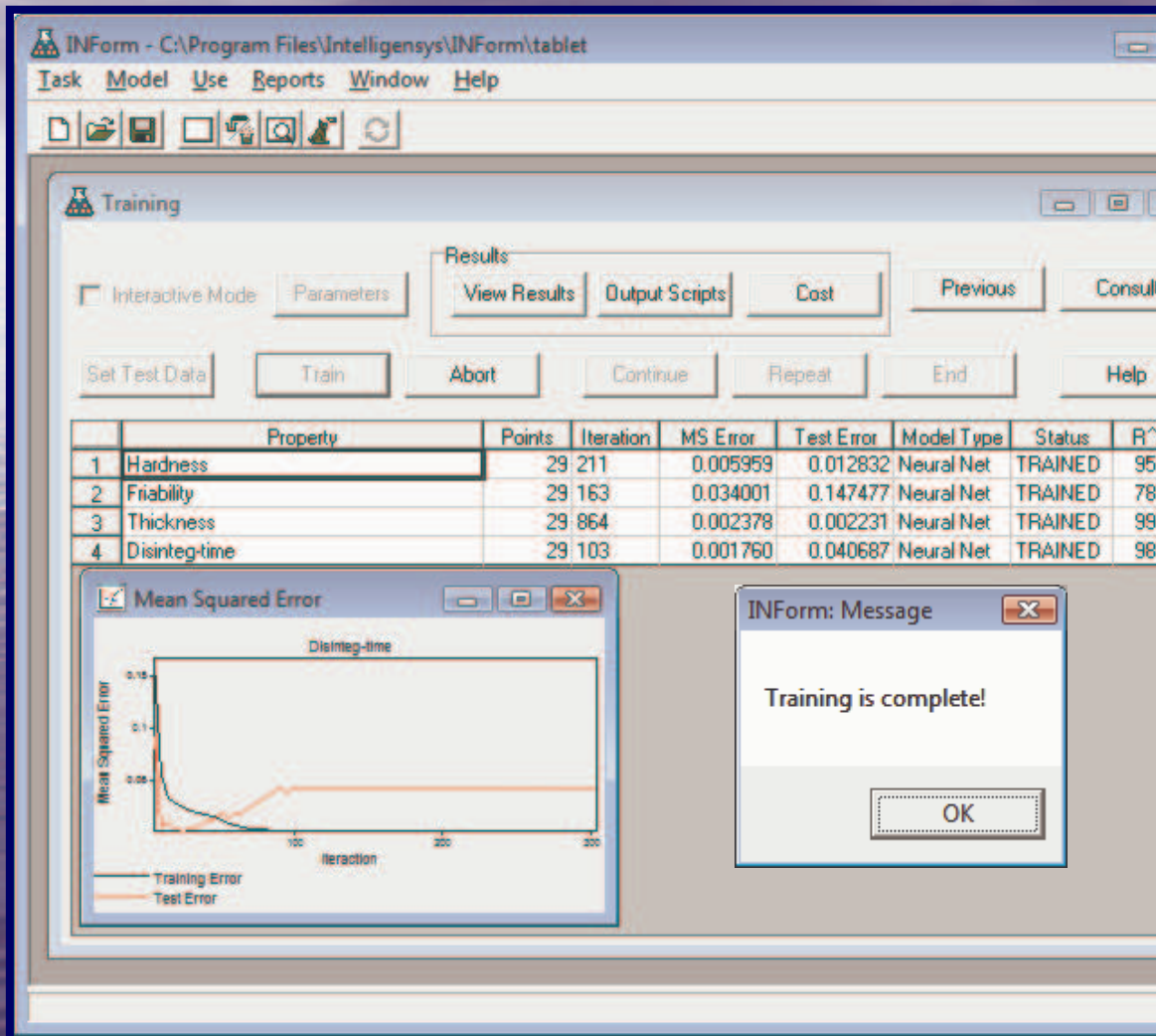
The background spreadsheet shows columns A through J with data for various parameters like Diluent, Lactose, Diltab, PVP%, Binder-addn, Gran-equip, and High Shear M.

Pressing the **Set Test Data** button on the training screen gives the Set Test Data screen shown here.

Press the Options button to get the choices you can make for the selection.

When you press **OK** on the Test Data Options, the data will be split into Training Data and Test Data.

Training



A single model is developed For each property.

MS (mean-squared) error tells you how good the fit is, to training data.

Test error tells you how well the model is predicting for withheld 'test' data

ANOVA R² value is shown once model has been developed

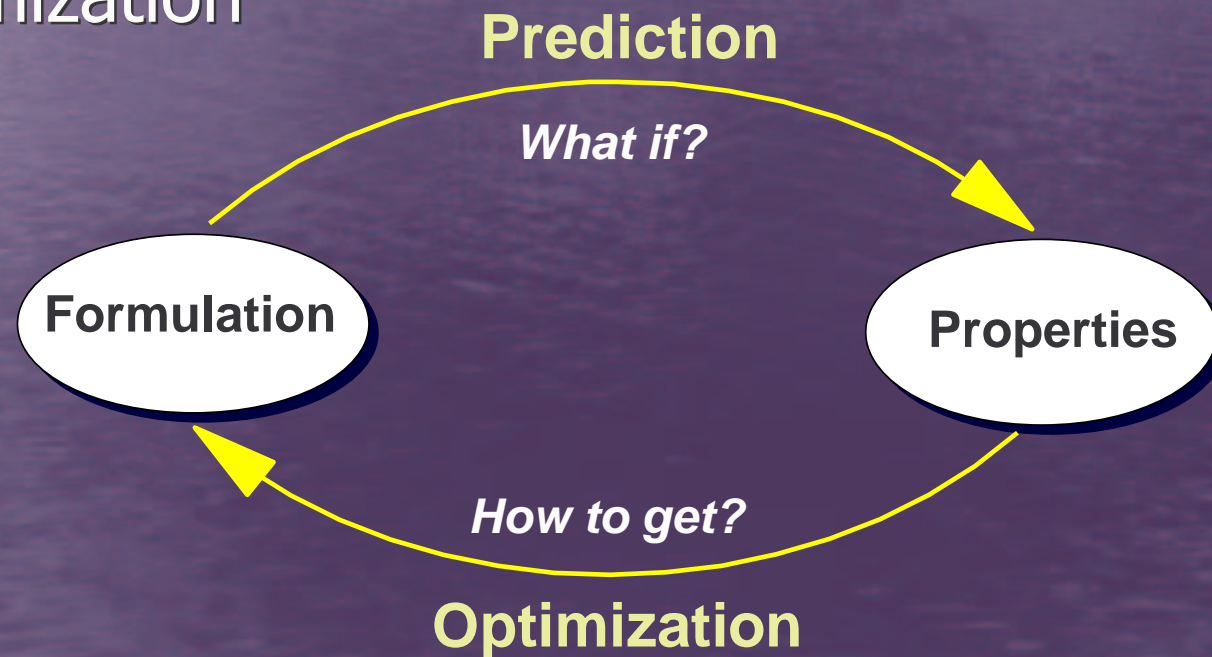
Click on **Consult** to move on to the next screen, where you can use the models.

Progress so far

- You've imported the data
- And set the field types, saying which variables are inputs and which are outputs
- You've set up 'test data' for validating the models
- And developed the models (assessing them to make sure they accurately represent the cause-and-effect relationships)
- Now, you can go on to *use* the models, for prediction and optimization

Using the model

- Two main options
 - Prediction: 'What if'
 - Optimization



The Consult screen

INForm - C:\Program Files\Intelligensys\INForm\tablet - [Model Consult]

Task Model Use Reports Window Help

Ingredients	Value
Diluent	lactose
Diluent%	0.0000
PVP%	0.0000
Binder-addn	dry
Gran-equip	fluidised bed

Properties	Actual	Predict
Hardness	0.0000	
Friability	0.0000	
Thickness	0.0000	
Disinteg-time	0.0000	

Predict View Data

3D Graph Explore

Optimize

Best Match

Sensitivity

Log

Add to

View

Training

Help

Label

Main features

Best Match – data retrieval from existing data

Predict – use Given ingredients – model predictions will be shown in Found properties

Optimize – gives the Optimization screens

'What if' predictions

The screenshot shows the INForm software interface. On the left, the 'Ingredients' table lists trial formulation parameters. On the right, the 'Properties' table shows actual and predicted values for various properties. A 'Predict' button is highlighted with a blue arrow pointing to a callout box.

Ingredients	Value
Diluent	lactose
Diluent%	46.0000
PVP%	2.0000
Binder-addn	wet
Gran-equip	high shear mixini

Properties	Actual	Predicted
Hardness	7.1700	6.9053
Friability	0.9200	0.4691
Thickness	3.3610	3.3633
Disinteg-time	161.0000	291.4521

Label :21 (index 21)

Your trial formulation

Prediction from the models

These results were found using the models, by pressing the **Predict** button

Visualizing Results

The screenshot shows the INForm software interface. The main window displays a table of ingredients and their values, and a table of properties with actual and predicted values. A callout box highlights the '3D Graph' and 'Explorer' buttons, explaining that they allow for graphical visualization of results, including 2D graphs and contour plots.

Ingredients	Value
Diluent	lactose
Diluent%	46.0000
PVP%	2.0000
Binder-addn	wet
Gran-equip	high shear mixi

Properties	Actual	Predicted
Hardness	7.1700	6.9053
Friability	0.9200	0.4691
Thickness	3.3610	3.3633
Disinteg-time	161.0000	291.4521

3D Graph and Explorer let you look At your results graphically. 2D graphs And contour plots can also be produced Using the 3D Graph button, as the next slide shows.

Buttons visible in the interface: Predict, View Data, 3D Graph, Explorer, Optimize, Best Match, Sensitivity, Log (Add to, View), Training, Help.

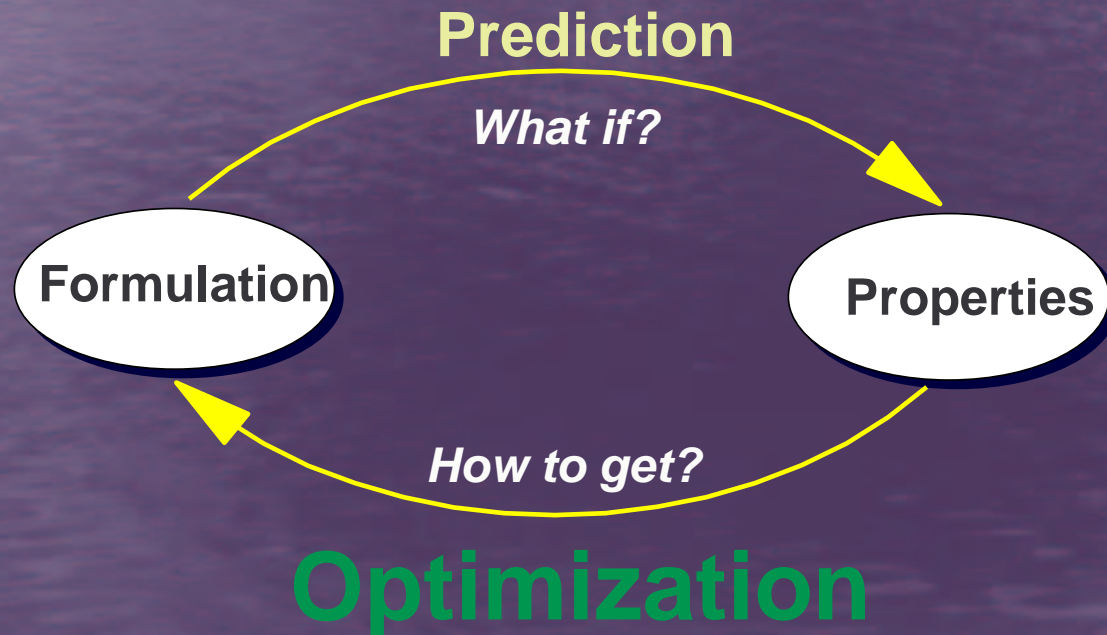
Label :21 (index 21)

The rest of the picture...

- Visualizations can help to understand the model
- Predictions can be useful to save you time
- But one of the real benefits of INForm comes from performing a multi-objective optimization
 - Allows you to balance conflicting goals
 - Saves wasted time and effort by showing you the best overall formulation

Optimization in INForm

- Uses the models in conjunction with an optimization technique
 - Genetic algorithms



Genetic algorithms

- 'Survival of the fittest' for possible solutions
- Especially suited to complex situations where there may be many possible 'local' solutions
- Requires a criterion of 'fitness' – how well the formulation meets your objectives
 - Desired values for each property
 - Relative importance of each property

Setting Up Optimization

The screenshot shows the 'INForm - C:\Program Files\Intelligensys\INForm\tablet2 - [Optimizer Configuration]' window. It features a menu bar (Task, Model, Use, Reports, Window, Help) and a toolbar. A table lists four properties: Hardness, Friability, Thickness, and Disinteg-time, each with a weight of 1.00 and specific Min, Mid1, Mid2, and Max values. A 'Desirability Function' column is also present. At the bottom, there are buttons for 'Set Values', 'Show Plot', 'Constraints', 'Save', 'Restore', 'OK', 'Cancel', and 'Help'.

	Property	Weight	Min	Mid1	Mid2	Max	Desirability Function
1	Hardness	1.00	3.84	8.42	8.42	13.00	Tent
2	Friability	1.00	0.08	1.99	1.99	3.90	Tent
3	Thickness	1.00	2.81	3.11	3.11	3.40	Tent
4	Disinteg-time	1.00	161.00	840.50	840.50	1520.00	Tent

Screen is ready to accept your requirements for properties, with default values taken from your data

Weights are relative importance of each property

This screen is obtained by pressing the **Optimize** button on the main **Consult** screen

Setting Optimization Targets

The screenshot shows the INForm Optimizer Configuration window. The main table lists properties and their optimization targets:

Property	Weight	Min	Mid1	Mid2	Max	Desirability Function
1 Hardness	1.00	3.84	10.00	8.42	13.00	Up
2 Friability	1.00	0.08	1.99	1.99	3.90	Tent
3 Thickness	1.00	2.81	3.11	3.11	3.40	Up
4 Disinteg-time	1.00	161.00	840.50	840.50	1520.00	Down

Callouts in the image:

- A blue box labeled "Desired values and ranges" has an arrow pointing to the table.
- A blue box labeled "Set any constraints (e.g. sum=100) for ingredients" has an arrow pointing to the "Constraints" button.
- Three diagrams illustrate desirability functions: "Up" (increasing), "Tent" (peak), and "Down" (decreasing).

Buttons at the bottom: Set Values, Show Plot, Constraints, Save, Restore, OK, Cancel, Help.

Relative importance of properties

The screenshot shows the 'Optimizer Configuration' window in INForm. The table below lists the properties and their weights. A blue oval highlights the 'Weight' column. A blue box contains the following text:

Weights on scale of
1 to 10

10 for most important
1 for least important

	Property	Weight	Min	Mid1	Mid2	Max	Desirability Function
1	Hardness	8.00	3.84	10.00	10.00	13.00	Up
2	Friability	5.00	0.08	1.99	1.99	3.90	Down
3	Thickness	1.00	2.81	3.11	3.11	3.40	Flat
4	Disinteg-time	10.00	1.00	240.00	240.00	1520.00	Down

Buttons at the bottom: Set Values, Show Plot, Constraints, Save, Restore, OK, Cancel, Help

Main Optimization Screen

Ingredients	Value	Integer	Fixed
1 Diluent	0.00	<input type="checkbox"/>	<input type="checkbox"/>
2 Diluent%	0.00	<input type="checkbox"/>	<input type="checkbox"/>
3 PVP%	0.00	<input type="checkbox"/>	<input type="checkbox"/>
4 Binder-addn	0.00	<input type="checkbox"/>	<input type="checkbox"/>
5 Gran-equip	0.00	<input type="checkbox"/>	<input type="checkbox"/>

Property	Value	Desirability
1 Hardness	0.00	0.00
2 Friability	0.00	0.00
3 Thickness	0.00	0.00
4 Disinteg-time	0.00	0.00

Initial Guess Parameters Optimize Close

Use Givens Abort Help

Total Desirability Searching...
Best 0.0 0 100

Values that must be integers can be fixed

Select starting point for optimization

Once the 'desirabilities' (target values) and 'weights' (relative importance) are set up, then you can start the optimization.

Values can be fixed to be integers, or to take values specified on the Consult screen (which are filled into the value field).

Completion of Optimization

- When Optimization is complete, and you close the window, the best formulation (ingredients and properties) are copied automatically to the Found columns on the Consult screen
- On the Consult screen, you can do things like a sensitivity analysis, or graph your results, too.

Understanding models

- GEP modelling technique gives models in the form of mathematical equations
- Both GEP and neural network models can be visualized (for example, response surfaces where inputs are varied and response is visualized)

3D graphs – response surfaces

3D Graph Setup

X Axis: Sucrose %
Avicel %
Aerosil %
Aerosol %

Y Axis: Sucrose %
Avicel %
Aerosil %
Aerosol %

Z Axis: Bulk density
Flowability
Viscosity
Sedimentation %
Redispersibility %

Minimum: 30 Minimum: 1 Extended Z Scale
Maximum: 60 Maximum: 2 Minimum: 0
Points: 10 Points: 10 Maximum: 1

Auto Z Scale
 Z grid at 0

Output As:
 Plot
 Contour
 Report
 Matrix

No. Contours: 10

Points on Plot
 Show All Points

OK
Cancel
Help

Pressing the 3D Graph button on the Consult hub gives the 3D Graph setup

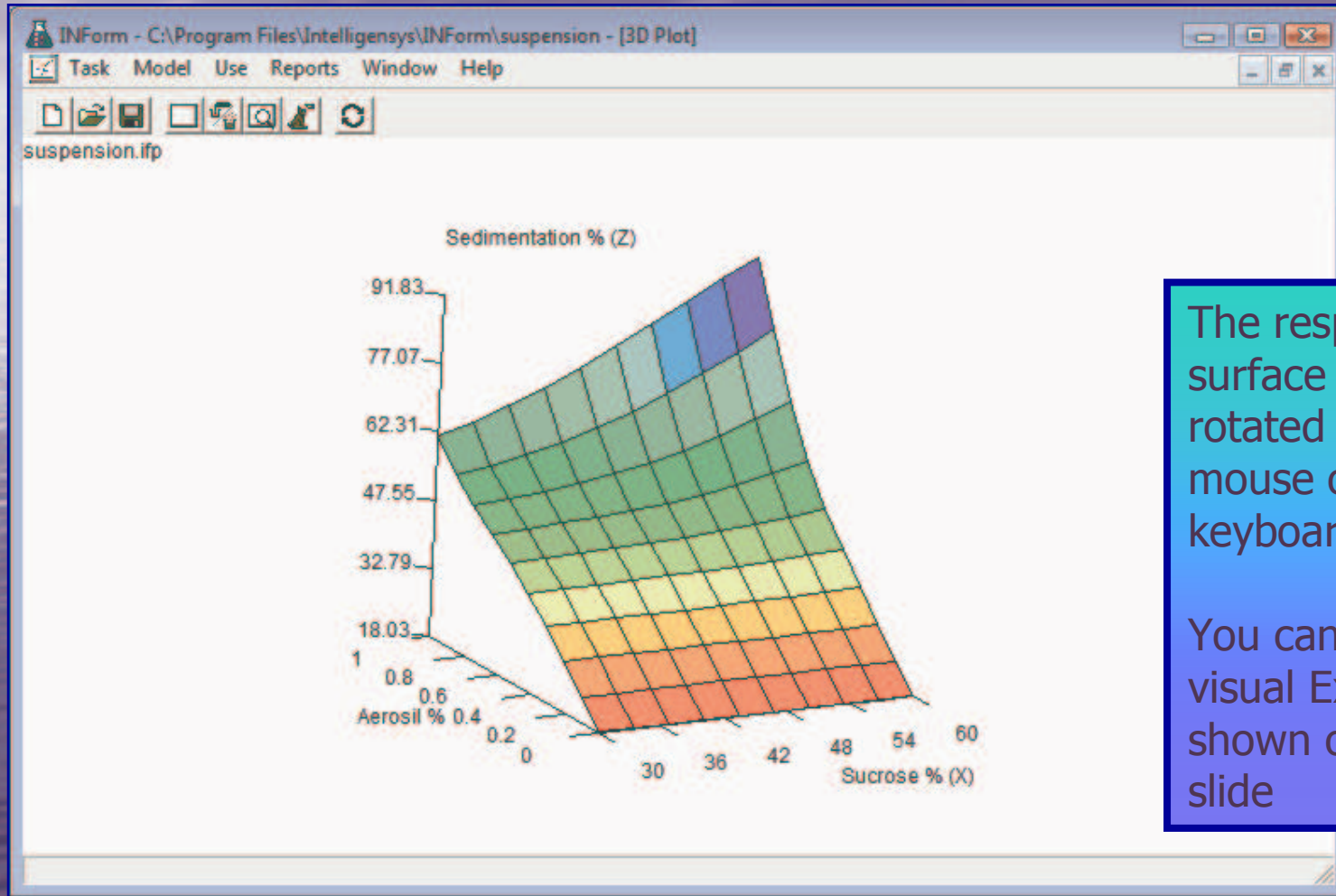
Here you can pick 2 inputs and one output

'Hidden' variables can take 'given' or 'found' values

You can select the scales for the plots, including extending the z axis

Contour plots and tab-delimited Report files can also be produced

3D Graphs – response surfaces



The response surface can be rotated using the mouse or by keyboard strokes

You can also use the visual Explorer, shown on the next slide

Visual Explorer

The screenshot displays the INForm software interface. The main window is titled "INForm - C:\Program Files\Intelligensys\INForm\suspension". Below the menu bar (Task, Model, Use, Reports, Window, Help) is a toolbar with various icons. The central area is dominated by the "3D Plot Surface Explorer" window, which contains a table of ingredients and their values, and a 3D surface plot.

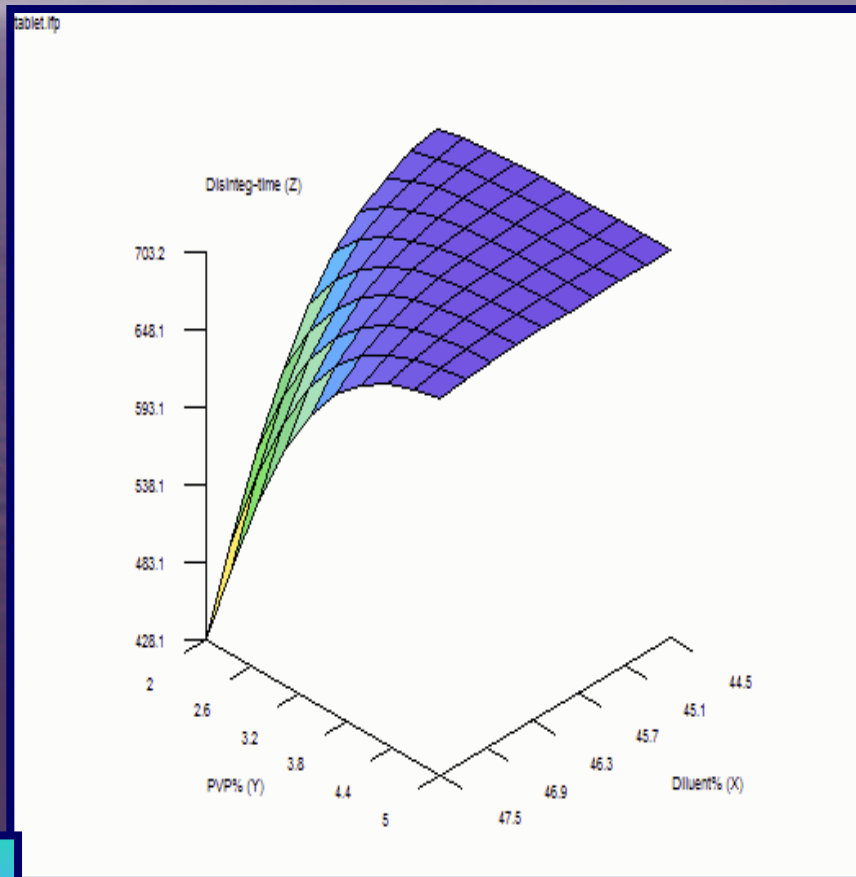
Ingredient	Value	Minimum	Maximum
Aerosil %	0.6400	0.0000	1.0000
Aerosol %	0.0000	0.0000	0.1000

The 3D plot shows "Sedimentation % (Z)" on the vertical axis, ranging from 46.18 to 60.51. The horizontal axes are "Avicel % (Y)" and "Sucrose % (X)". A callout box with a blue gradient background and a blue border contains the text: "The slider bar allows you to change one of the variables, and see what effect the change has on the properties – interactively!". A blue arrow points from this callout to a slider bar for "Aerosil %" which is currently set to 0.00. Below the slider, a label reads "Label:17 (index 17)".

Other features of INForm

- Graphical display (response surfaces)
 - Easy to copy to reports and presentations
- Input and output screens spreadsheet-enabled for easy data import and export
- 'Log' for important results
- Sensitivity analysis to test for formulation/process robustness

An integrated solution for formulation and process modelling and optimization



Remember...

- INForm is versatile
 - It works on your own data, so as long as you have cause-and-effect information hidden in that data, INForm can find this information and enable you to use it easily
- INForm does not require specialist artificial intelligence expertise
 - Defaults have been tested so that they are generally reliable for formulation problems
 - You are given full information that enables you to assess your models

INForm

- Can be supplied as a networkable licence, allowing anyone on your LAN to access the software and share results
- Is backed by a full range of training, maintenance and support options
- Is continually being developed in collaboration with customers and academic groups worldwide

Expand Your Horizons

- For more information, contact Intelligensys

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