



ADVANCED PROCESS  
MODELLING FORUM  
LONDON  
20–21 APRIL 2016

# Global System Analysis

From uncertainty quantification to risk management

Costas Pantelides – Managing Director

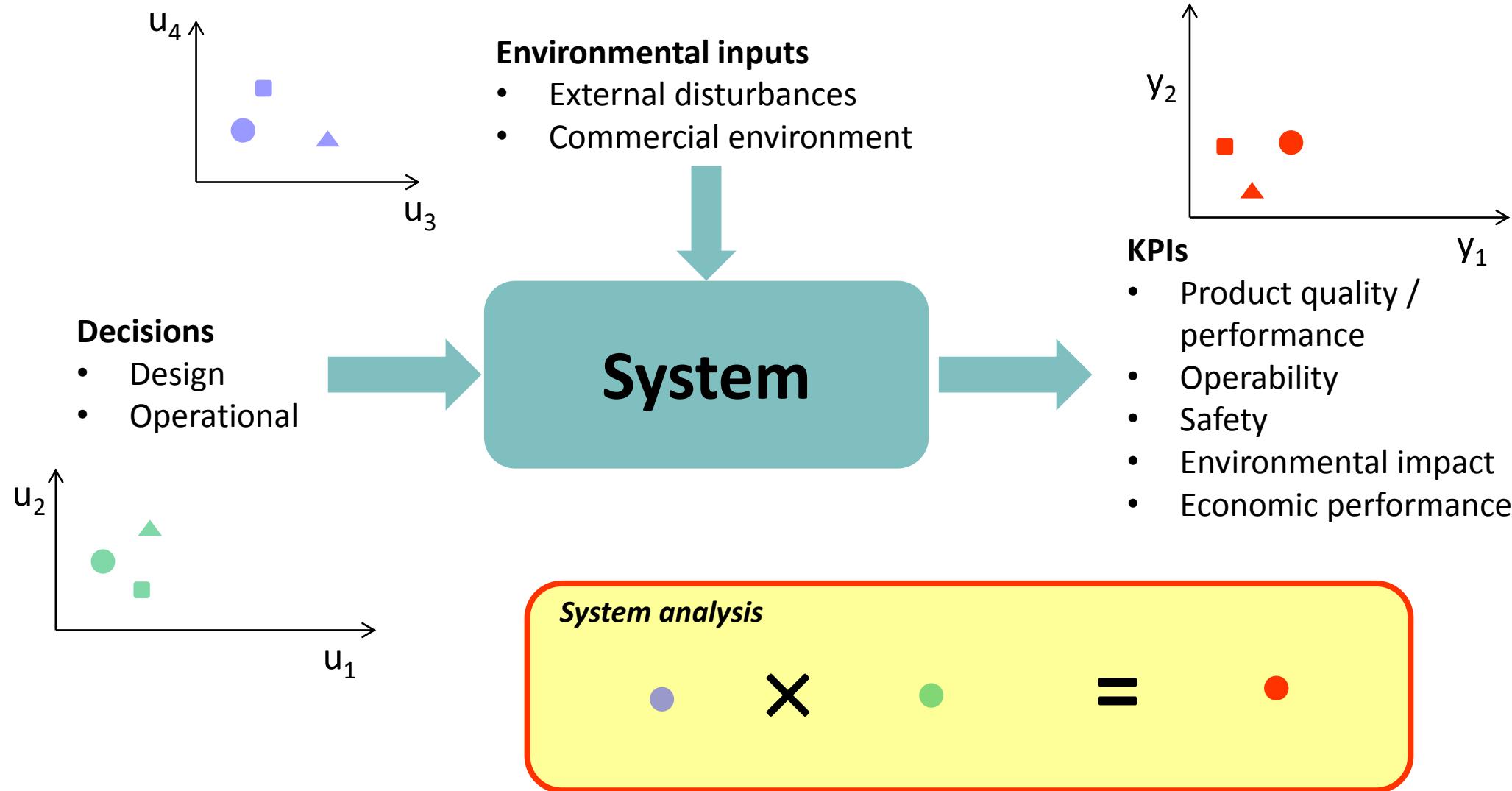


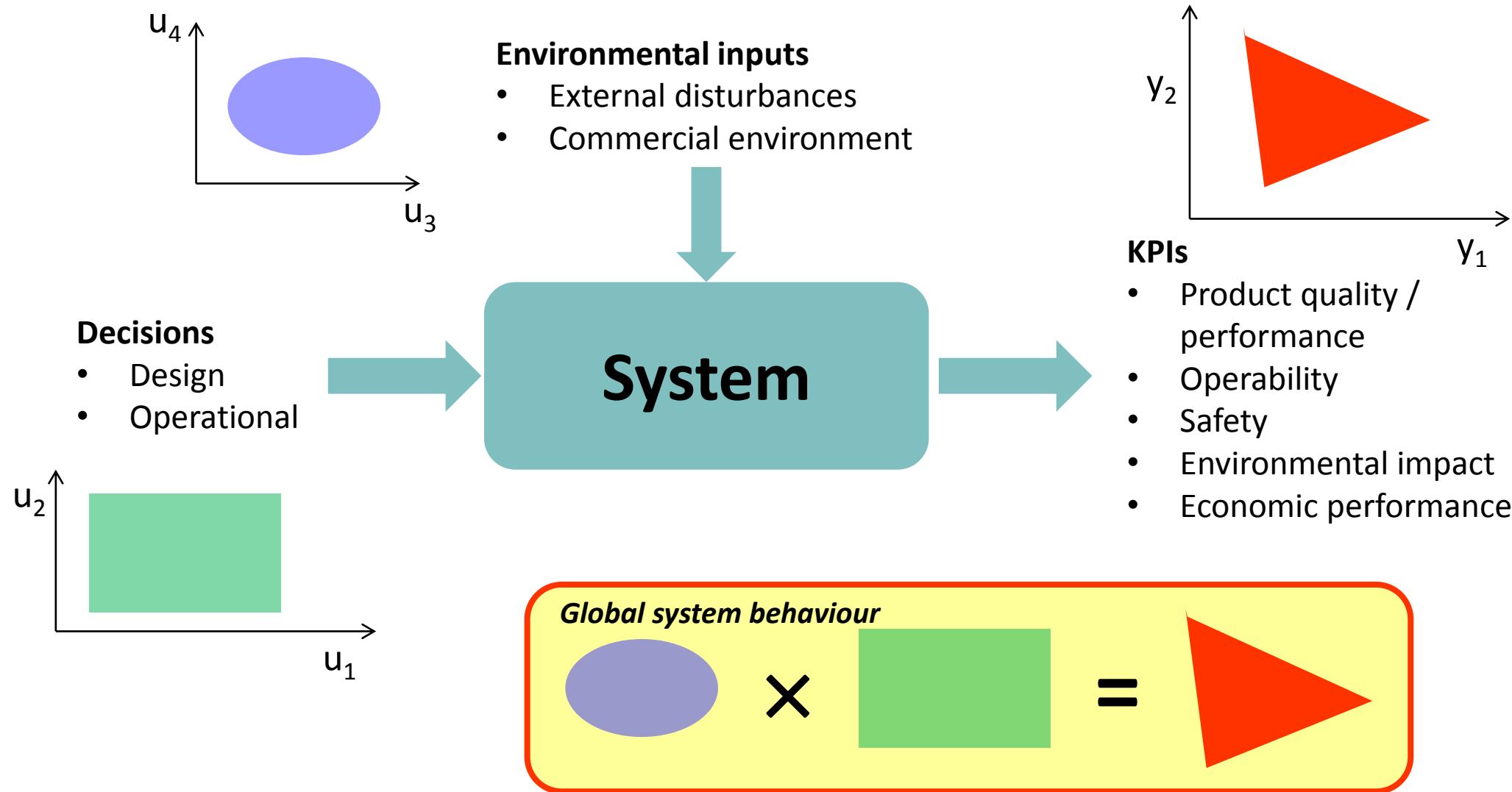
- From point calculations to global system behaviour
- Global system analysis in gPROMS
- Examples
  - Air Separation unit
  - Tablet dissolution
- Concluding remarks

# From point calculations to global system behaviour

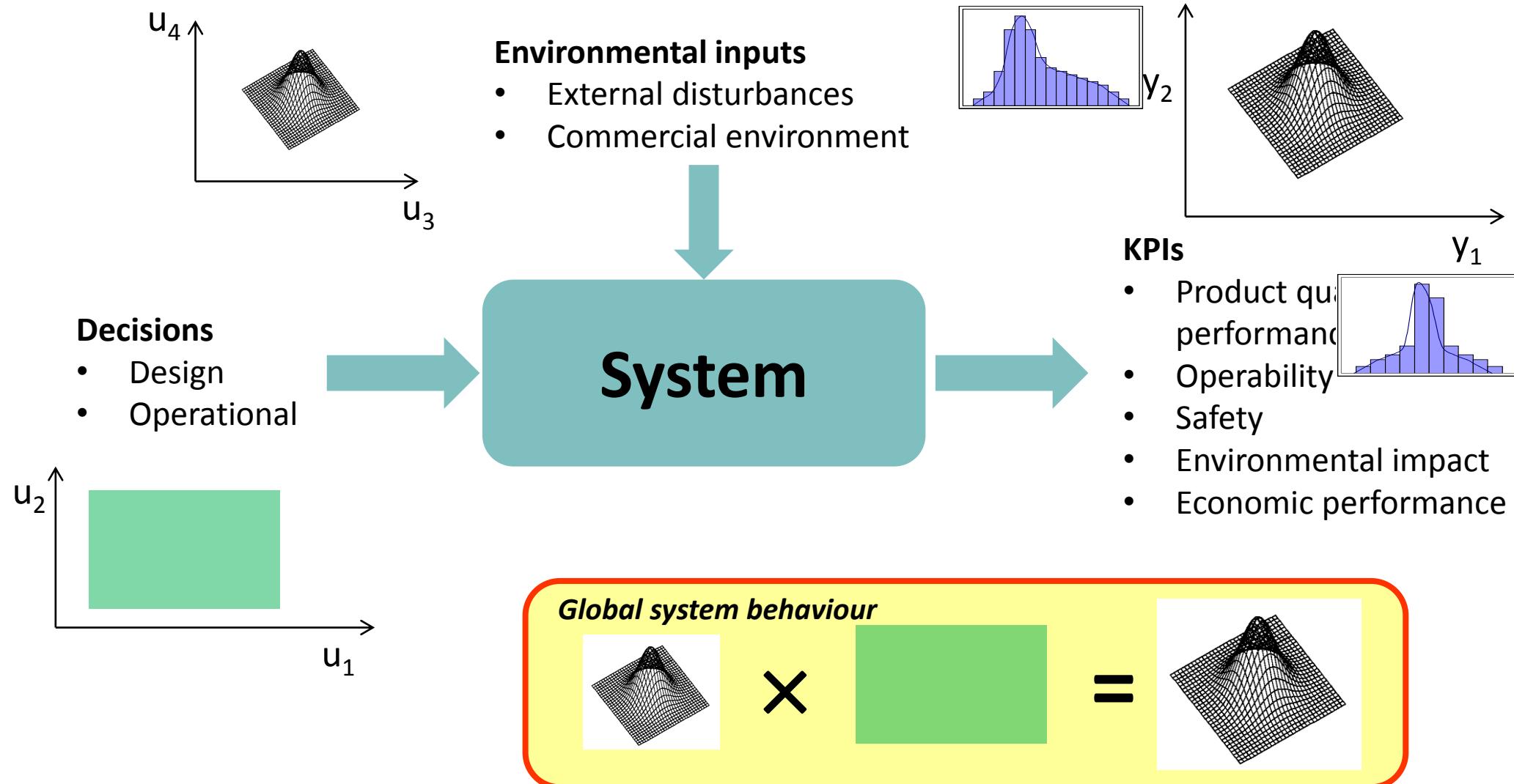


# System analysis

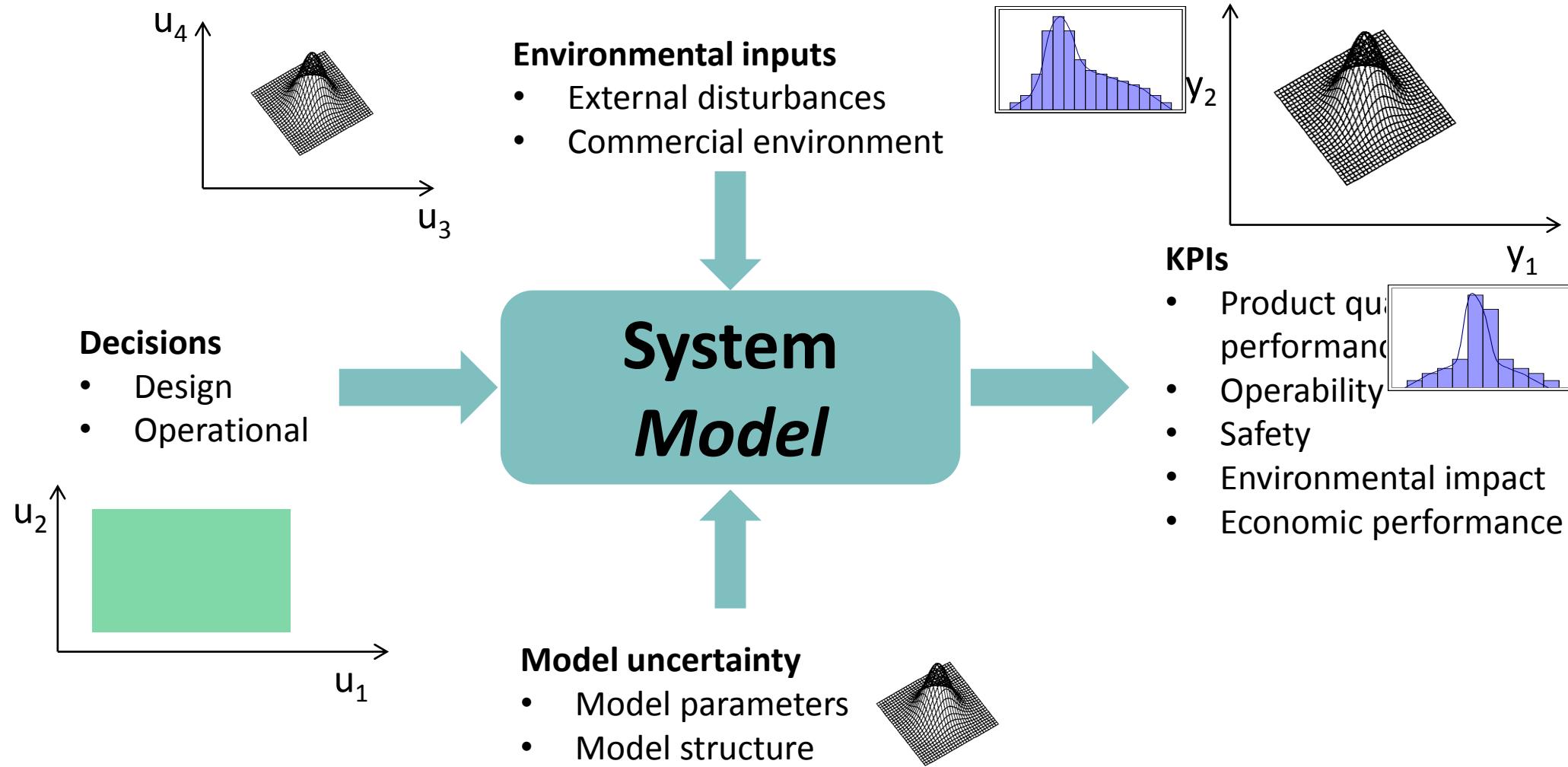




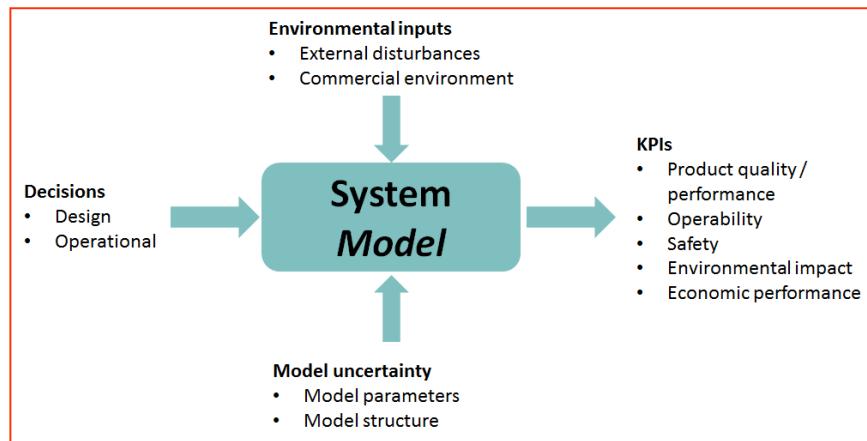
# Global system behaviour in an uncertain world



# Model-based analysis of global system behaviour



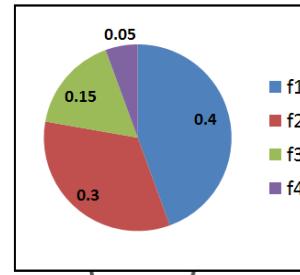
# Model-based global system analysis in an uncertain world



## Key objectives

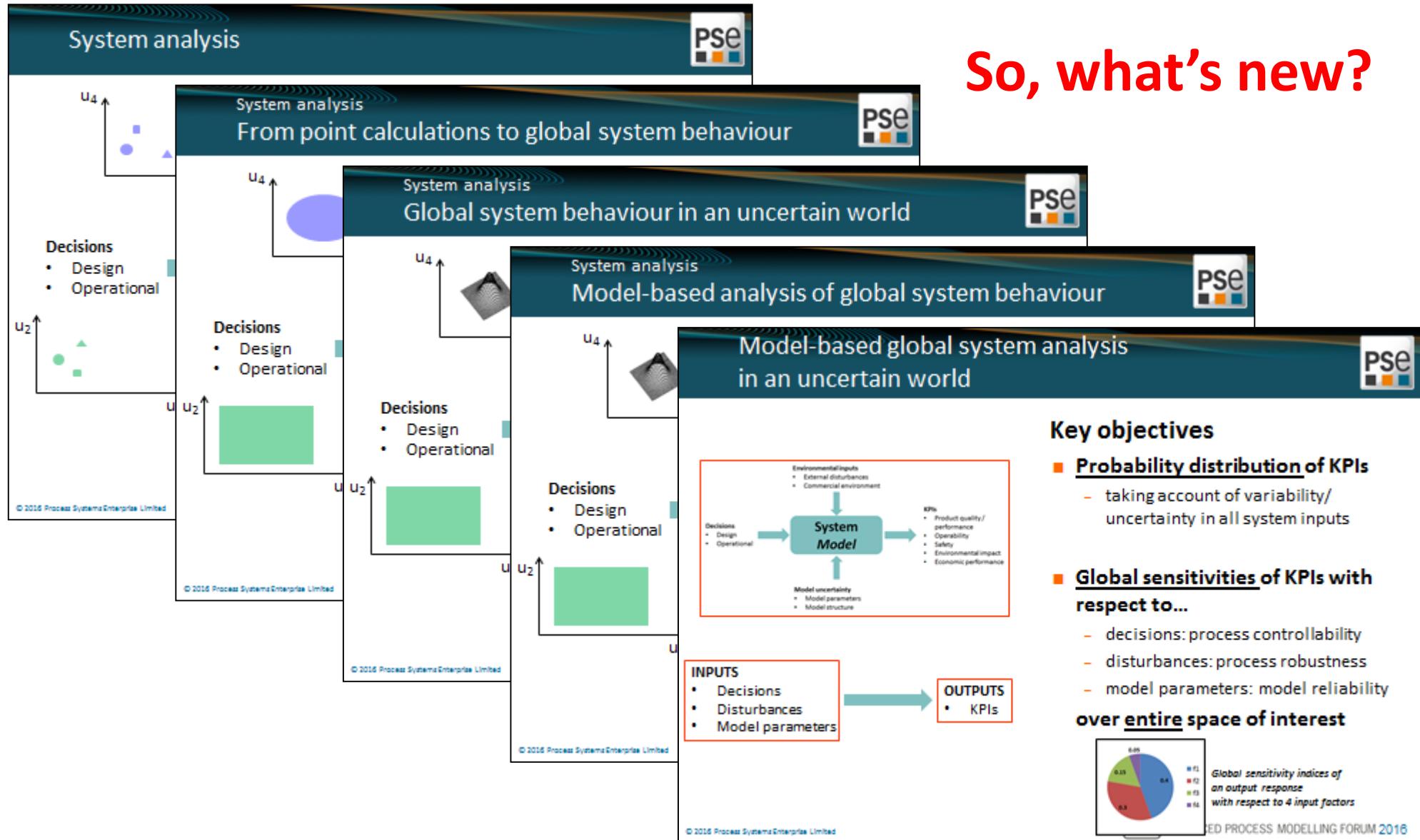
- **Probability distribution of KPIs**
  - taking account of variability/uncertainty in all system inputs
- **Global sensitivities of KPIs with respect to...**
  - decisions: process controllability
  - disturbances: process robustness
  - model parameters: model reliability

**over entire space of interest**



*Global sensitivity indices of an output response with respect to 4 input factors*

# So, what's new?



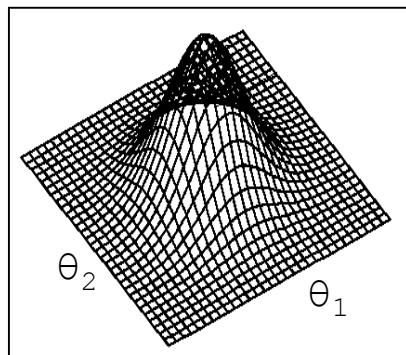
# Global System Analysis in gPROMS



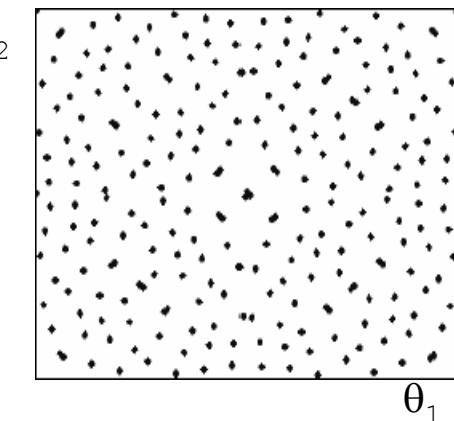
# Global System Analysis

## A general tool for the gPROMS platform

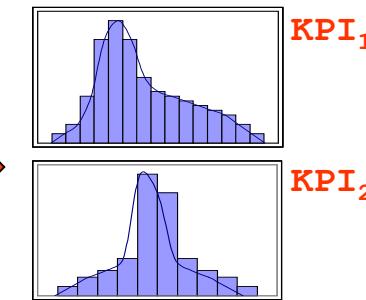
### I. Inputs (“Factors”)



### II. Sampling



### III. Outputs (“Responses”)



### A collaborative R&D project (June 2014-May 2016)

- Project leader : PSE
- Consortium : AstraZeneca, GSK, Pfizer
- Funding (partial) : £988k (~\$1.5m) by InnovateUK

### A fundamental capability within the gPROMS platform

- Directly applicable to any gPROMS model in any gPRODUCT
  - (e.g. ModelBuilder, ProcessBuilder, ....)
- Initial version to be released as part of gPROMS v4.3

# Global System Analysis in gPROMS

## GSA development team



### GSA User Interface



Kate Haddow



Elzbieta Abel

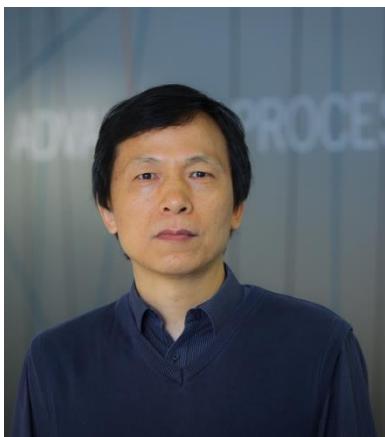


Cristi Marius-Pop



Daren Grant  
GSA Team Leader

### GSA in gPROMS Kernel



Yuzhao Lu



Xenia Kleniati



Ed Figura



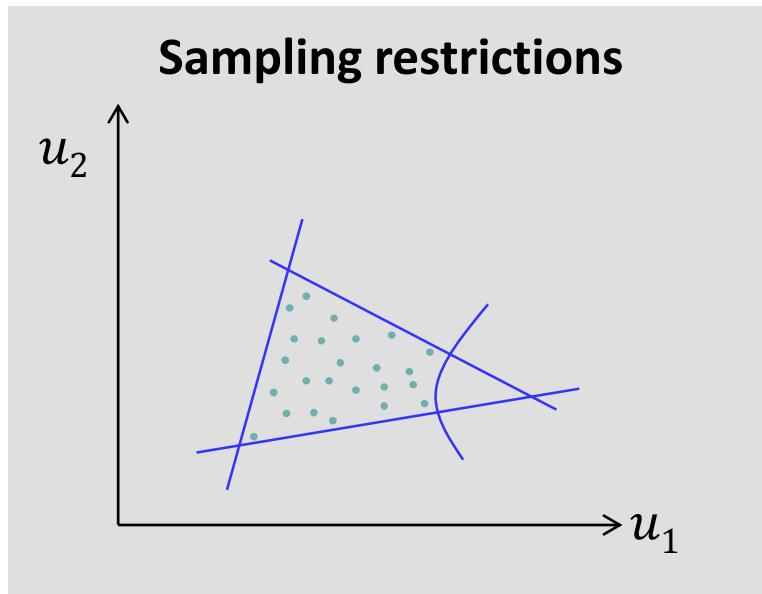
ADVANCED PROCESS MODELLING FORUM 2016

## I. Input factors

**Factors:** user-selected subset of the ASSIGNED variables in the PROCESS

## Deterministic Factors

- Multiple case study (“scenarios”) capability



## Probabilistic

- Discrete vs. continuous probability distributions
- Univariate distributions: uniform, normal, *lognormal\**, ....
- Multivariate: normal
  - specified in terms of covariance matrix

\*Feature not in v1.0

## II. Output responses

**Responses:** user-selected subset of the *unASSIGNed* variables in the PROCESS

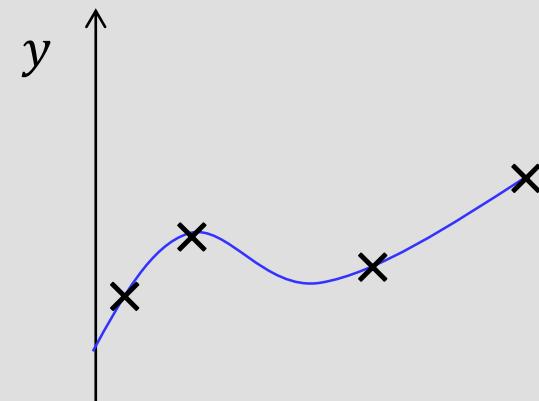
### Steady-state models

- Steady-state values of specified variables

### Dynamic models

- Values of specified variables
  - at final point
  - *on user-specified time grid(s)*\*

#### Timed responses



\*Feature not in v1.0

### III. Types of analysis

#### 1. Elementary Effects analysis

- Identify which of the input factors have a non-negligible effect on at least one of the output responses

**→ eliminate unimportant factors from further consideration**

#### 2. Uncertainty analysis

- Determine probability distribution of output responses

**→ quantify uncertainty → risk in model-based decisions**

#### 3. Sensitivity analysis

- Compute global sensitivity indices of each response with respect to each factor or combination of factors

- first- & higher-order sensitivity indices

- Apportion variability of outputs to variability of inputs

**→ target risk management actions**

# IV. Execution

## ■ Sample generation

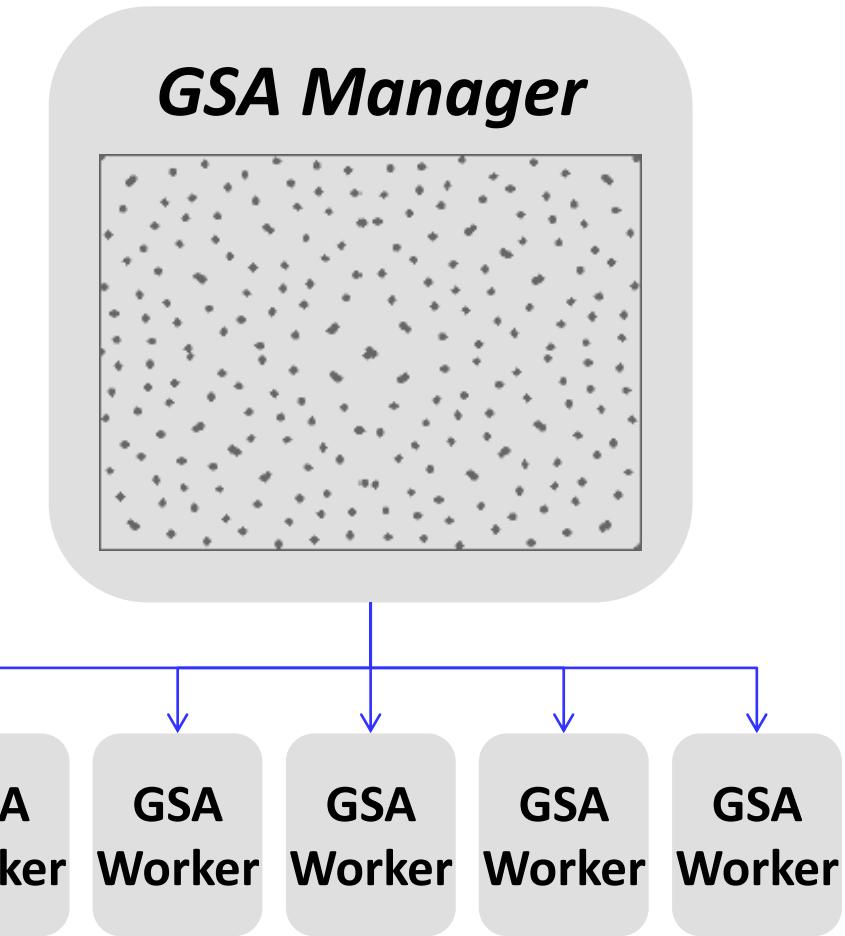
- Pseudo-random points
- Quasi-random points
  - Low-discrepancy Sobol' sequences

## ■ Parallelized execution of multiple samples

- multicore processors and/or *multiprocessor clusters\**
- transparent to user
- resilient, failure-tolerant execution
  - aim to complete number of sample points specified by user

## ■ Results

- Record values of factors & responses at each sampling point
  - failure points also recorded for subsequent analysis
- HDF5 file format
  - scalable to huge data sets

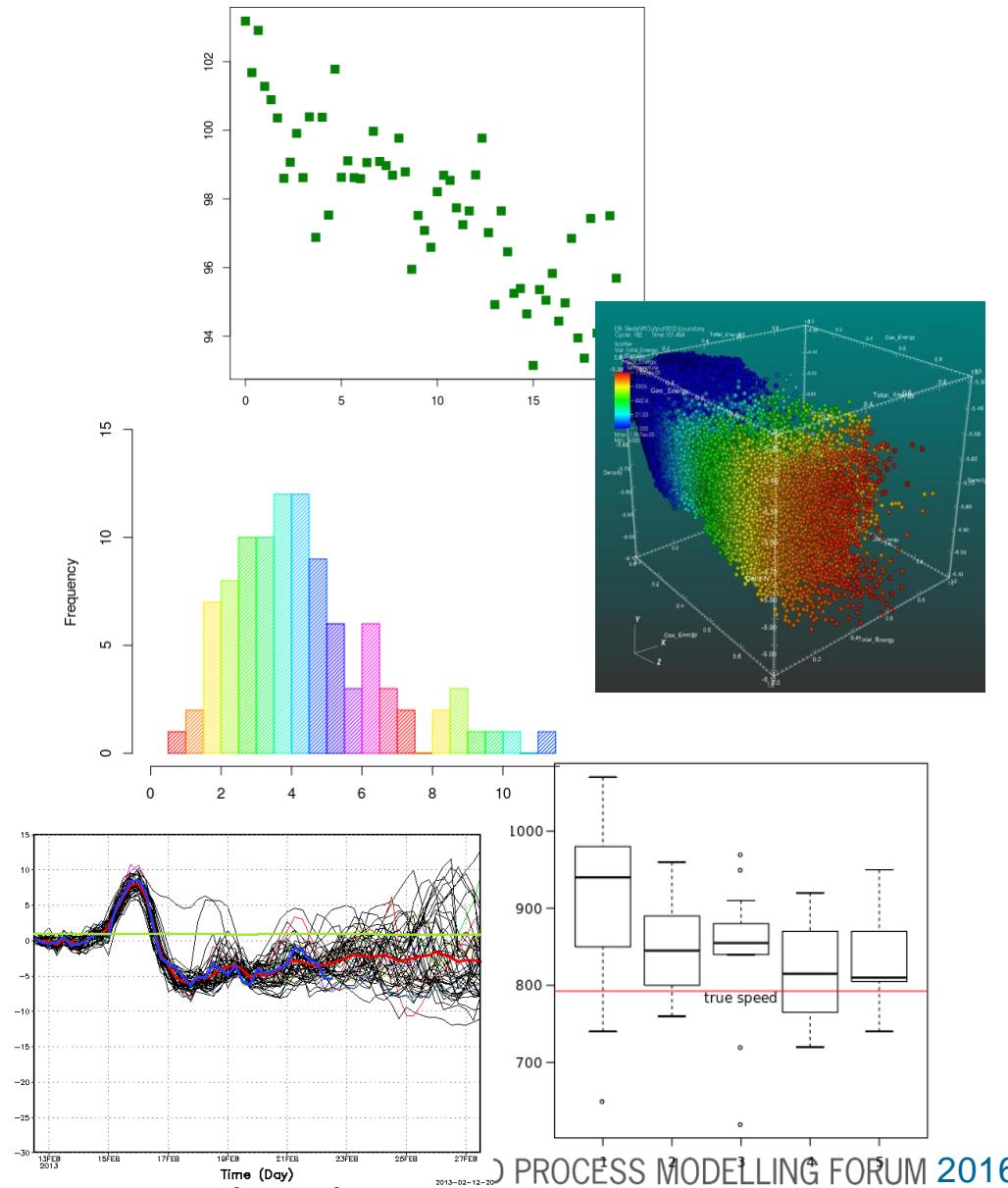


\*Feature not in v1.0

## V. Results analysis

- Extensive facilities for analysing and presenting large data sets
  
- Data filtering mechanisms
  - *System Constraints\**
  
- Graphs & tables
  - created on the fly
  - organized in Reports
  - can be stored within original project file for future use

*\*Feature not in v1.0*

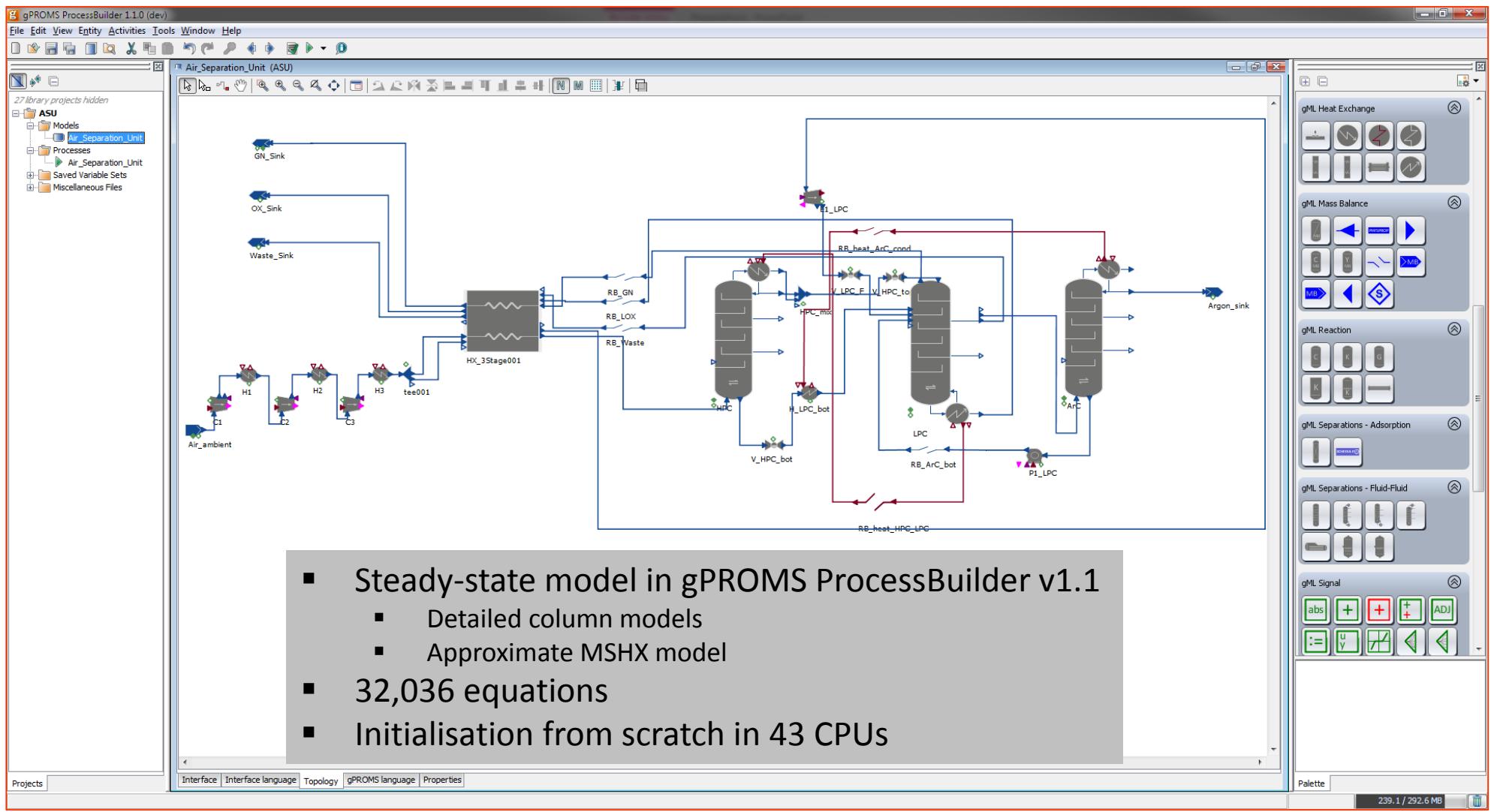


# Global System Analysis

## Example #1: Air Separation Unit



# Global System Analysis in gPROMS ASU model



# Specifying the input factors for Global System Analysis

In this particular ASU model, the nitrogen production rate and the oxygen product purity are both specified  
→ may act as input factors

Use 500 sample points to sample the input factor space

The screenshot shows the gPROMS ModelBuilder interface. On the left, the 'Projects' browser displays a library project named 'ASU-GSA-Praxair-New-SVS' containing 'Models', 'Processes', 'Simulate\_ASU', 'Global System Analysis', 'Saved Variable Sets', and 'Miscellaneous Files'. The main workspace shows a complex process flow diagram for an 'Air\_Separation\_Unit' with various components like compressors, heat exchangers, and separators. Below the workspace is a 'Factors' dialog box. It lists two factors: 'Nitrogen\_Production\_Rate' (Variable in model: 'adj\_spec002 → Target value', Unit: 'See d...', Lower b...: '13.0', Upper b...: '15.0', Probability distribution: 'Uniform distribution') and 'Oxygen\_Purity' (Variable in model: 'LPC → Bottom product purity', Unit: 'mol/mol', Lower b...: '0.985', Upper b...: '0.999', Probability distribution: 'Uniform distribution'). The dialog also includes sections for 'Sampling restrictions' and 'Number of samples' (Number of discrete deterministic cases: '1', Number of uncertainty scenarios/probability distribution samples: '500', Total realisations of base activity to be calculated: '500'). At the bottom, tabs for 'General', 'Factors', 'Responses', 'GSA language', and 'Properties' are visible. The status bar at the bottom shows 'dareng@localhost:/Desktop' and 'gPROMS ModelBuilder 4.3.0 (dev...)'. The right side of the interface features a palette with various icons for annotations, gML Basics, gML Connectivity, gML Control, and gML Flow Transportation.

# Specifying the output responses of interest

Applications gcom-psenterprise-application-modelbuilder-Main

File Edit View Entity Activities Tools Window Help

gPROMS ModelBuilder 4.3.0 (dev) - debug mode

Mon 12:41 Daren Neil Grant

Air\_Separation\_Unit (ASU-GSA-Praxair-New-SVS)

Annotations

gML Basics

gML Connectivity

gML Control

gML Flow Transportation

Palette

Projects

General Factors Responses GSA language Properties

dareng@localhost:/Desktop gPROMS ModelBuilder 4.3.0 (dev...)

27 library projects hidden

- ASU-GSA-Praxair-New-SVS
  - Models
  - Processes
  - Simulate\_ASU
  - Global System Analysis
  - AnalyseAsu
  - Saved Variable Sets
  - Miscellaneous Files

**Responses**

Enabled	Name	Variable in model	Unit	Tags
<input checked="" type="checkbox"/>	Argon_Production_Rate	Argon_sink → Molar flowrate	kmol/h	
<input checked="" type="checkbox"/>	Nitrogen_Purity	GN_Sink → Molar fraction ("NITROGEN")	mol/mol	
<input checked="" type="checkbox"/>	Oxygen_Production_Rate	OX_Sink → Molar flowrate	kmol/h	
<input checked="" type="checkbox"/>	Reboiler_duty_LPC	ColumnKPIs → Reboiler heat duty ("LPC")	kJ/s	
<input checked="" type="checkbox"/>	Reflux_ratio_molar_ArC	ColumnKPIs → Reflux molar ratio ("ArC")		
<a href="#">Add new</a>				

Kernels: 0 223.7 / 509.4 MB 1 / 4

# Selecting the type of GSA to be performed

gPROMS ModelBuilder 4.3.0 (dev) – debug mode

File Edit View Entity Activities Tools Window Help

Applications gpm-pseenterprise-application-modelbuilder-Main Mon 12:50 Daren Neil Grant

**Air\_Separation\_Unit (ASU-GSA-Praxair-New-SVS)**

27 library projects hidden

- ASU-GSA-Praxair-New-SVS
- Models
- Processes
- Simulate\_ASU
- Global System Analysis
- AnalyseASu
- Saved Variable Sets
- Miscellaneous Files

**AnalyseASu (ASU-GSA-Praxair-New-SVS)**

Base activity for analysis: Simulate\_ASU

Type of analysis to be performed: Uncertainty analysis

Method to be used for analysis:

- Monte-Carlo
  - Derivative-based global sensitivity measures
  - Kucherenko-RodriguezFernandez-Pantelides-Shah
  - Elementary effects
  - Campolongo-Cariboni-Saltelli
  - Variance-based sensitivity indices
  - Sobol-Saltelli
  - Kucherenko-Tarantola-Annoni
- Monte-Carlo
 

The Monte Carlo method performs multiple model evaluations (simulations) with deterministically and/or probabilistically selected model input. The results of these evaluations are then used to determine the uncertainty in the model output.

The Monte Carlo method is appropriate for complex models in which large uncertainties are associated with the input variables. The selection of ranges and distributions for the input variables under consideration (**factors**) must be performed carefully because it can have a large impact on the estimated ranges and distributions for the output variables under consideration (**responses**).

Sample generation method: Quasi-random (Sobol) sampling

Composite Tasks

- IF - perform an action conditionally
- PARALLEL - start a set of parallel actions
- SEQUENCE - insert a sequence of actions
- WHILE - repeat a set of actions in a loop while an expression is true

Elementary Tasks

- CONTINUE - operate undisturbed for a specified period and/or until a condition is met
- MESSAGE - write a message to the output screen
- MONITOR - change which output values are received
- REASSIGN - change the value or time variation of an input variable
- REINITIAL - instantaneously move the system to a different point in the trajectory
- REPLACE - change the set of variables that are specified
- RESETRESULTS - discard all previous data that was transmitted to a defined output channel
- RESTORE - restore the values from a saved state
- SAVE - save the current values of the system
- STOP - halt the simulation

Perform an uncertainty analysis  
→ focus on probability distributions of responses of interest

Choose quasi-random (rather than pseudo-random) sampling to achieve better coverage of the input factor space

dareng@localhost:~/Desktop gPROMS ModelBuilder 4.3.0 (dev...) 220.2 / 508.9 MB 1 / 4

# Global System Analysis in gPROMS

## Execution of GSA calculation – I



Applications Terminal

File Edit View Tools Window Help

gPROMS ModelBuilder 4.3.0 (dev) - debug mode

Mon 13:16 Daren Neil Grant

Air\_Separation\_Unit (ASU-GSA-Praxair-New-SVS)

Execution Output (AnalyseAsu\_20151207\_13L441)

Show messages to level 2 and update Infrequently Update

Using Multiflash dynamic library version 4.3.51, April  
From gPROMS FO interface version 4.3.0 Build 00000000, built Nov 30 2015  
Requesting MF\_MULTIFLASH\_MODULE license from server.  
License granted by server(s) licserv1.  
Foreign Object initialisation completed successfully.

Constructing the system...  
Creating parameters...  
Creating variables...  
Creating selectors...  
Creating streams...  
Applying assignments...  
Applying initial selectors...  
Identity Elimination: SCHEDULE section scan...  
Identity Elimination: performing elimination...  
Building equations and State Transition Networks...  
Creating Jacobian expressions...  
25% ...  
50% ...  
75% ...  
100%  
Creating system reports...  
System construction details  
System summary  
Parameters: 36244  
Variables: 33908  
User defined: 69652  
Eliminated: -35744  
Selectors: 324  
Residual expressions: 28932  
Jacobian expressions: 127617 in active branches, 129304 total  
Clear eliminated constraints  
Performing Structural Analysis...

Structural analysis report

Variables: 33908  
Unknown: 28932  
Algebraic: 28932  
Differential: 0  
Known (assigned): 4976

Equations: 28932  
Model equations: 28932  
Initial conditions: 0

Index of the problem: 0  
Original problem is well posed  
Loaded "GSANetCDF.so".

Spawning 5 GSA workers...

STDOUT: Requesting gSRV1 license from server.  
STDOUT: License granted by server(s) licserv1.  
STDOUT: gPROMS (R) - Version 4.3.0 (x64) for Linux 3.10.0-229.11.1.el7.x86\_64 x86\_64 Nov 30 2015  
STDOUT: general PROcess Modelling System  
STDOUT: Copyright (c) 1997-2015 Process Systems Enterprise Ltd

dareng@localhost:~/Desktop

File Edit View Search Terminal Tabs Help

dareng@localhost:~/Desktop dareng@localhost:~/Desktop

top - 13:16:15 up 1:34, 3 users, load average: 4.61, 1.77, 0.84  
Tasks: 275 total, 9 running, 266 sleeping, 0 stopped, 0 zombie  
%Cpu(s): 83.6 us, 4.0 sy, 0.0 ni, 12.4 id, 0.0 wa, 0.0 hi, 0.0 si, 0.0 st  
KiB Mem : 8172948 total, 2609004 free, 4381936 used, 1182008 buff/cache  
KiB Swap : 2097148 total, 2097148 free, 0 used. 3542236 avail Mem

PID USER PR NI VIRT RES SHR %CPU %MEM TIME+ COMMAND

6280	dareng	20	0	770856	378956	30892	R	100.0	4.6	1:18.30	gGSAWorker.exe
6271	dareng	20	0	773152	381368	30888	R	99.7	4.7	1:19.02	gGSAWorker.exe
6272	dareng	20	0	770708	378924	30892	R	99.7	4.6	1:19.03	gGSAWorker.exe
6276	dareng	20	0	769072	375908	30880	R	99.7	4.6	1:18.45	gGSAWorker.exe
6284	dareng	20	0	773148	381360	30892	R	99.7	4.7	1:18.31	gGSAWorker.exe
3078	dareng	20	0	1749496	317776	39272	S	13.0	3.9	6:56.64	gnome-shell
1346	root	20	0	312316	66						
6246	dareng	20	0	1098016	333						
4588	dareng	20	0	6171512	882						
3069	dareng	20	0	321704	6						
1	root	20	0	58860	6						
2	root	20	0	0	0						
3	root	20	0	0	0						
5	root	0	-20	0	0						

Behind the scenes view from Task Manager:  
5 "GSA worker" processes launched & executing in parallel on multicore laptop machine

Output Properties

Kernels: 1 251.0 / 485.3 MB 1 / 4

dareng@localhost:~/Desktop gPROMS ModelBuilder 4.3.0 (dev...)

ASU model size statistics  
(printed just after start of execution)

# Global System Analysis in gPROMS

## Execution of GSA calculation – II

Applications gom-psenterprise-application-modelbuilder-Main

File Edit View Tools Window Help

Air\_Separation\_Unit (ASU-GSA-Praxair-New-SVS)

Execution Output (AnalyseAsu\_20151207\_131441)

Completed 30% [sample 150/500]

Completed 35% [sample 175/500]

Execution of 500 samples now in full swing:  
Throughput of ~4-5 converged ASU simulations per elapsed second on standard laptop machine

dareng@localhost:~/Desktop

File Edit View Search Terminal Tabs Help

dareng@localhost:~/Desktop

top - 13:16:39 up 1:35, 3 users, load average: 4.97, 2.08, 0.97  
Tasks: 275 total, 7 running, 268 sleeping, 0 stopped, 0 zombie  
%Cpu(s): 84.0 us, 3.7 sy, 0.0 ni, 12.3 id, 0.0 wa, 0.0 hi, 0.1 si, 0.0 st  
KiB Mem : 8172948 total, 2604700 free, 4385944 used, 1182304 buff/cache  
KiB Swap: 2097148 total, 2097148 free, 0 used. 3538012 avail Mem

PID	USER	PR	NI	VIRT	RES	SHR	S	%CPU	%MEM	TIME+	COMMAND
6280	dareng	20	0	770856	378956	30892	R	100.0	4.6	1:42.31	gGSAWorker.exe
6276	dareng	20	0	772228	378936	30880	R	99.7	4.6	1:42.47	gGSAWorker.exe
6271	dareng	20	0	773152	381368	30888	R	99.3	4.7	1:43.00	gGSAWorker.exe
6272	dareng	20	0	772224	380312	30892	R	99.3	4.7	1:43.04	gGSAWorker.exe
6284	dareng	20	0	773148	381360	30892	R	99.3	4.7	1:42.10	gGSAWorker.exe
3078	dareng	20	0	1749496	317						
1346	root	20	0	312316	66						
6246	dareng	20	0	1098016	333						
4588	dareng	20	0	6171572	882						
41	root	20	0	0							
74	root	rt	0	0							
3243	dareng	20	0	186832	5						
3278	dareng	20	0	419184	10696	4776	S	0.3	0.1	0:03.33	prlsga
5732	dareng	20	0	130152	1948	1260	R	0.3	0.0	0:03.25	top

All 5 "GSA worker" processes being kept fully busy with sample point evaluations

Projects Interface Interface language Topology gPROMS language Properties

Output Properties

Kernels: 1 265.7 / 485.3 MB

dareng@localhost:~/Desktop gPROMS ModelBuilder 4.3.0 (dev...)

# Global System Analysis in gPROMS

## Typical results



Applications g.com-psenterprise-application-modelbuilder-Main

gPROMS ModelBuilder 4.3.0 (dev) - debug mode

File Edit View Tools Window Help

27 library projects hidden

- ASU-GSA-Praxair-New-SVS
- Models
- Air\_Separation\_Unit
- Processes
- Simulate\_ASU
- Global System Analysis
- AnalyseAsu
- Saved Variable Sets
- Air\_Separation\_Unit\_InitialGuess
- Miscellaneous Files
- AnalyseAsu\_20151207\_122221
- Original Entities
- Results
- System Analysis Results
- Input\_Factors
- KPI\_Statistics
- O2ProdRate
- O2pur\_ArProdRate
- Problem Description
- Execution Output

**KPI\_Statistics (AnalyseAsu\_20151207\_122221)**

Distribution Statistics Table

Variables	Expected Value	Std deviation	SI
Nitrogen_Production...	14.0006640625	0.575540850159775	0.06605
Oxygen_Purity	0.9920081484375	0.0040379156575041	5.0435
Argon_Production_R...	10.7977068629606	4.2011308359581	-4.941
Nitrogen_Purity	0.999998798635901	1.25581349214661E-6	-1.5666
Oxygen_Production...	1052.92532891396	110.148225692411	95.13
Reboiler_duty_LPC	5941.26767585156	859.773105744884	762.3
Reflux_ratio_molar_ArC	1857.7308217946	5638.10667270678	8111

**Distribution statistics for all input factors & output responses (formatting yet to be improved!)**

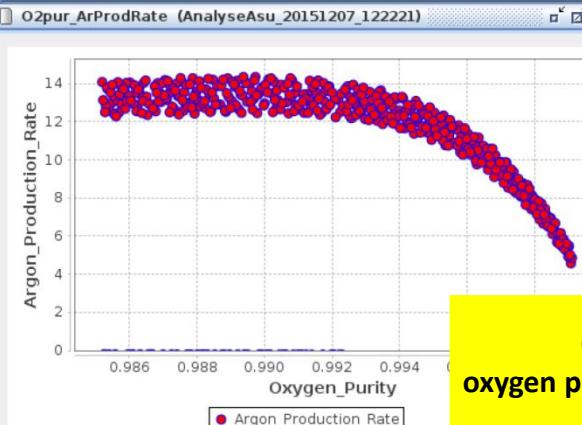
**O2pur\_ArProdRate (AnalyseAsu\_20151207\_122221)**

Scatter plot showing Argon\_Production\_Rate vs Oxygen\_Purity.

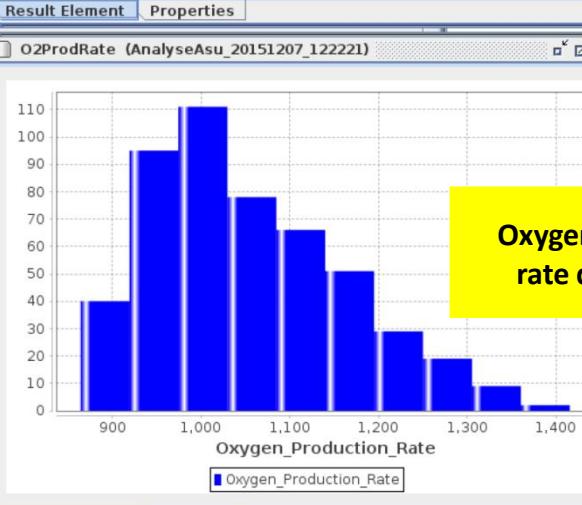
**Input\_Factors (AnalyseAsu\_20151207\_122221)**

Scatter plot showing Oxygen\_Purity vs Nitrogen\_Production\_Rate.

Scatter plot of the two input factors shows uniformity of domain coverage



Correlation between oxygen purity & argon production rate



Oxygen production rate distribution

# Global System Analysis

## Example #2: Tablet dissolution



# Global System Analysis in gPROMS

## USP<sup>II</sup> tablet dissolution model



gPROMS ModelBuilder 4.3.0 (dev) - gCOAS GSA

File Edit View Entity Activities Tools Window Help

USP<sub>II</sub>\_template (USP<sub>II</sub> template)

Global specifications

Please double click on the icon to enter:

- 1) Drug properties

Vessel

Please double click on the icon to enter:

- 1) Configuration
- 2) Media

Default specifications are made for:

- 1) Transit
- 2) Primary nucleation
- 3) Growth and dissolution
- 4) Bile salt partitioning
- 5) Diffusion

Simulation duration

Please double click on the icon to enter:

- 1) The length of time to simulate

Tablet

Please double click on the icon to enter:

- 1) Dosing schedule
- 2) Particle size distribution

To change to a different dosage form, right click on the icon and select "Change MODEL."

Solid type Neutral -

Molecular weight 267 g/mol

Intrinsic solubility 4 mg/mL

API dose mass 100 mg

D50 100 µm

USP<sub>II</sub> media Water -

USP<sub>II</sub> media volume 20 ml

- **Dynamic model in gCOAS**  
USP<sub>II</sub> vessel model  
Detailed transit, dissolution, precipitation and reaction kinetics
- **1692 equations**
- **5 CPUs solution time**



# Global System Analysis in gPROMS

## Specifying factors and responses



gPROMS ModelBuilder 4.3.0 (dev) - gCOAS GSA

File Edit View Entity Activities Tools Window Help

USP\_II (USP II Design Global Uncertainty Analysis Simple Example)

Factors

Enabled	Name	Variable in model	Unit	Lower bound	Upper bound	Probability distribution	Tags
<input checked="" type="checkbox"/>	D50	tablet001 → Location parameter ("Freeform")	μm	0.0	10000.0	Normal distribution	
<input checked="" type="checkbox"/>	Mass_dosed	tablet001 → Dose time and mass ("Active drug mass dosed (mg)",1)		0.0	1E20	Normal distribution	

Sampling restrictions

Enabled	Name

Number of samples

Number of discrete deterministic cases: 1

Number of uncertainty scenarios/probability distribution samples: 500

Total realisations of base activity to be calculated: 500

General Factors Responses GSA language Properties

GSA (USP II Design Global Uncertainty Analysis Simple Example)

Responses

Enabled	Name	Variable in model	Unit	Tags
<input checked="" type="checkbox"/>	Fraction_dissolved	Vessel001 → Fraction dissolved ("Freeform")		
<input checked="" type="checkbox"/>	API_concentration	Vessel001 → Total API liquid mass concentration	mg/mL	

Input factors of interest  
→ Mass dosed  
→ Particle size distribution D50

Use 500 sample points to sample the input factor space

Output responses of interest  
→ Fraction dissolved after 15 mins  
→ API concentration after 15 mins

Projects Interface Interface language Topology gPROMS language Properties

107.8 / 167.3 MB

# Global System Analysis in gPROMS

## Selecting type of global system analysis to be performed



gPROMS ModelBuilder 4.3.0 (dev) - gCOAS GSA

File Edit View Tools Window Help

7 library projects hidden

USP II Design Global Uncertainty Analysis

Models

Processes

Global System Analysis

GSA

GSA\_20160208\_115133

Original Entities

Results

System Analysis Results

Problem Description

Execution Output

Factor 1. D50

Factor 2. Tablet API mass dosed

Response 1. Tablet API mass dissolved after 15 minutes

Execution Output (GSA\_20160208\_115133)

Show messages to level 2

Structural analysis report

Variables: 1938

Unknown: 1639

Algebraic: 1586

Differential: 53

Known (assigned): 299

Equations: 1692

Model equations: 1639

Initial conditions: 53

Index of the problem: 1

Original problem is well posed

Loaded "GSANetCF.dll".

Spawning 3 GSA workers...

Sample generation method Quasi-random (Sobol) sampling

General Factors Responses GSA language Properties

Base activity for analysis USP\_II

Type of analysis to be performed Uncertainty analysis

Method to be used for analysis

Monte-Carlo

Derivative-based global sensitivity measures Kucherenko-Rodriguez-Fernandez-Pantelides-Shah

Elementary effects Campolongo-Cariboni-Saltelli

Variance-based sensitivity indices Sobol-Saltelli Kucherenko-Tarantola-Annoni

Monte-Carlo

The Monte Carlo method performs multiple model evaluations (simulations) with deterministically and/or probabilistically selected model input. The results of these evaluations are then used to determine the uncertainty in the model output.

The Monte Carlo method is appropriate for complex models in which large uncertainties are associated with the input variables. The selection of ranges and distributions for the input variables under consideration (*factors*) must be performed carefully because it can have a large impact on the estimated ranges and distributions for the output variables under consideration (*responses*).

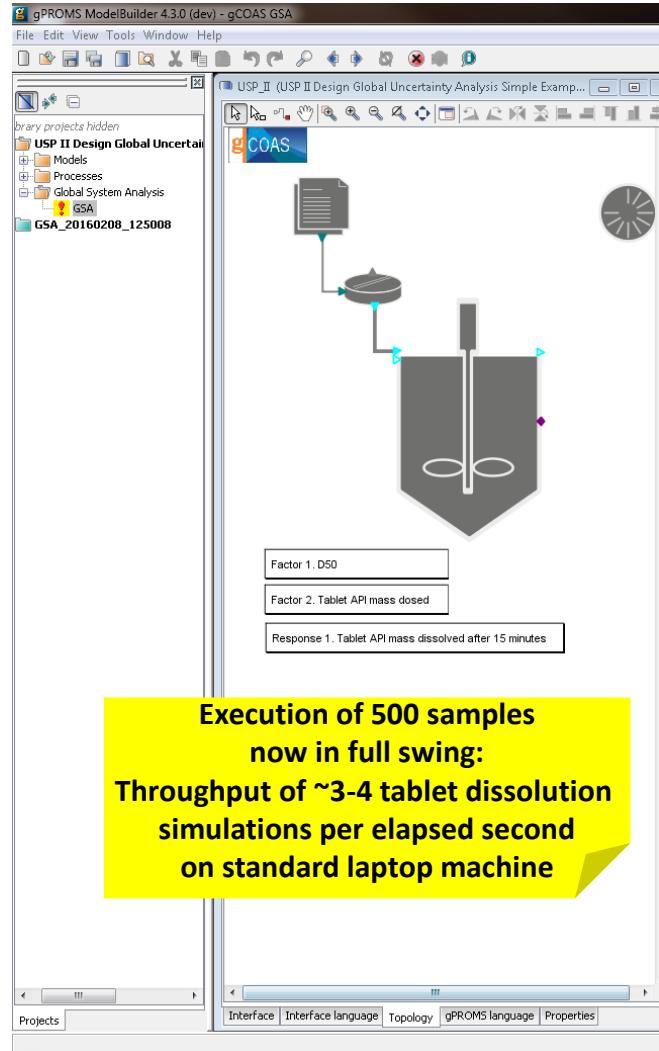
However, Monte Carlo methods can also be used with rather crude range and distribution assumptions as a first iteration, in order to identify the most important factors and to avoid spending a large effort characterising the uncertainty of variables that may have little impact on the ultimate outcome of the analysis.

The gPROMS platform implements standard Monte Carlo method with pseudo-random sequences and quasi-Monte Carlo with Sobol sequences for the sample generation. Quasi-random (Sobol) sequences fill the space more uniformly than pseudo-random ones and are proved more efficient for medium-size problems and a high number of samples. On the other hand, quasi-Monte Carlo behaves like standard Monte Carlo for high-dimensional problems and a moderate number of samples.

Choose  
quasi-random Sobol sampling  
→ achieve better coverage of the  
input factor space than  
with pseudo-random sampling

# Global System Analysis in gPROMS

## Execution of GSA calculation



## Execution of 500 samples now in full swing:

Throughput of ~3-4 tablet dissolution simulations per elapsed second on standard laptop machine

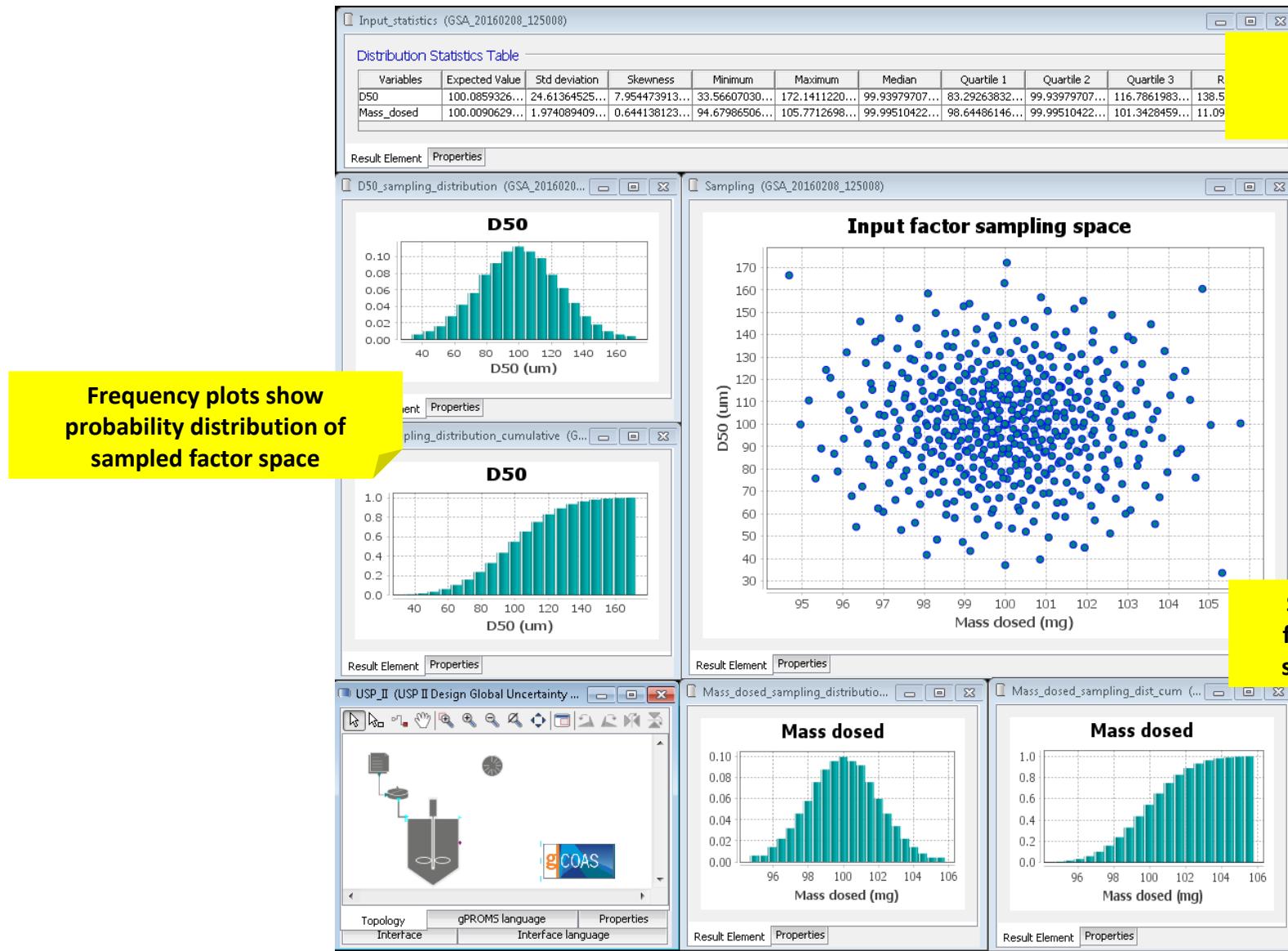
The screenshot shows the Windows Task Manager window with the 'Applications' tab selected. The main pane displays a list of running processes. A yellow box highlights the title bar and the 'Applications' tab. Below the table, there is a button labeled 'Show processes from all users'.

Image Name	User Name	CPU	Memory (...)	Description
gSAAWorker.exe	edwardc	25	83,412 K	gSAAWorker.exe
gSAAWorker.exe	edwardc	25	83,588 K	gSAAWorker.exe
gSAAWorker.exe	edwardc	21	82,748 K	gSAAWorker.exe
gObjectServer.exe	edwardc	00	57,020 K	gObjectServer.exe
gObjectServer.exe	edwardc	00	74,288 K	gObjectServer.exe
gSERVERcorba.exe	edwardc	00	113,940 K	gSERVERcorba.exe
hkcmd.exe	edwardc	00	2,992 K	hkcmd Module
igfpxers.exe	edwards	00	4,968 K	persistence Module
iusb3mon.exe *32	edwardc	00	2,020 K	Intel(R) USB 3.0 Monitor
javaw.exe	edwardc	02	489,980 K	Java(TM) Platform SE binary
LiquidFilesWindowsAge...	edwardc	00	16,176 K	LiquidFiles Windows Agent
MCPLaunch.exe *32	edwardc	00	332 K	Message Center Plus Scheduler
MobileAccess.exe	edwardc	00	30,316 K	MobileAccess
mplexec.exe	edwardc	00	3,468 K	Process manager for MPI applications

All 3 “GSA worker” processes  
being kept fully busy with  
sample point evaluations

Behind the scenes view  
from Task Manager:  
3 “GSA worker” processes  
launched & executing in parallel  
on multicore laptop machine

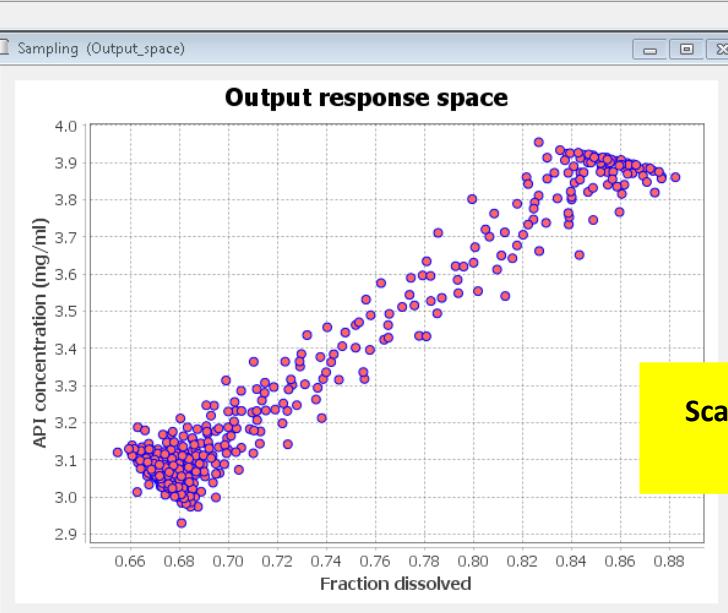
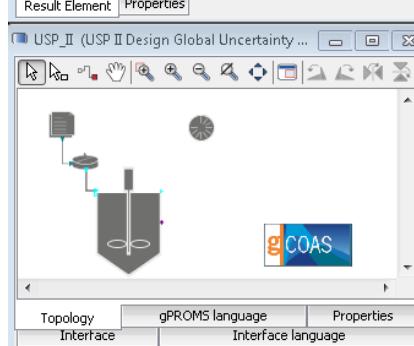
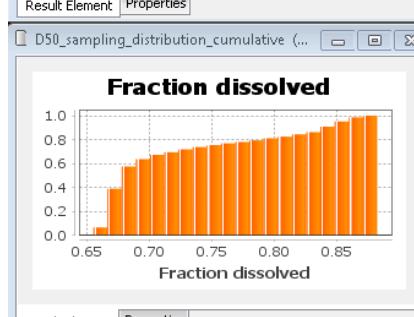
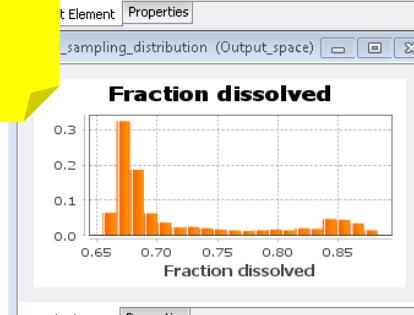
# Results analysis: input factor sampling space



# Results analysis: output response design space

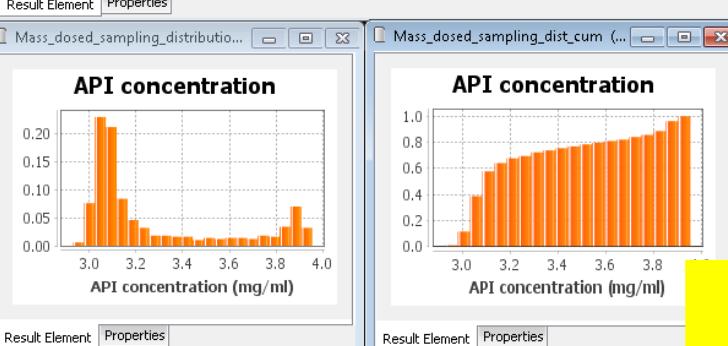
Distribution Statistics Table										
Variables	Expected Value	Std deviation	Skewness	Minimum	Maximum	Median	Quartile 1	Quartile 2	Quartile 3	Range
Fraction_dissolved	0.719875442...	0.067647427...	0.070949118...	0.654611907...	0.882372266...	0.682002538...	0.673065497...	0.682002538...	0.755173576...	0.227760358...
API_concentration	3.271903296...	0.30733596...	0.319799143...	2.930179782...	3.955019494...	3.110424484...	3.060314145...	3.110424484...	3.433437849...	1.024839711...

Fraction dissolved distribution



Distribution statistics for all output responses

Scatter plots for visualising response space

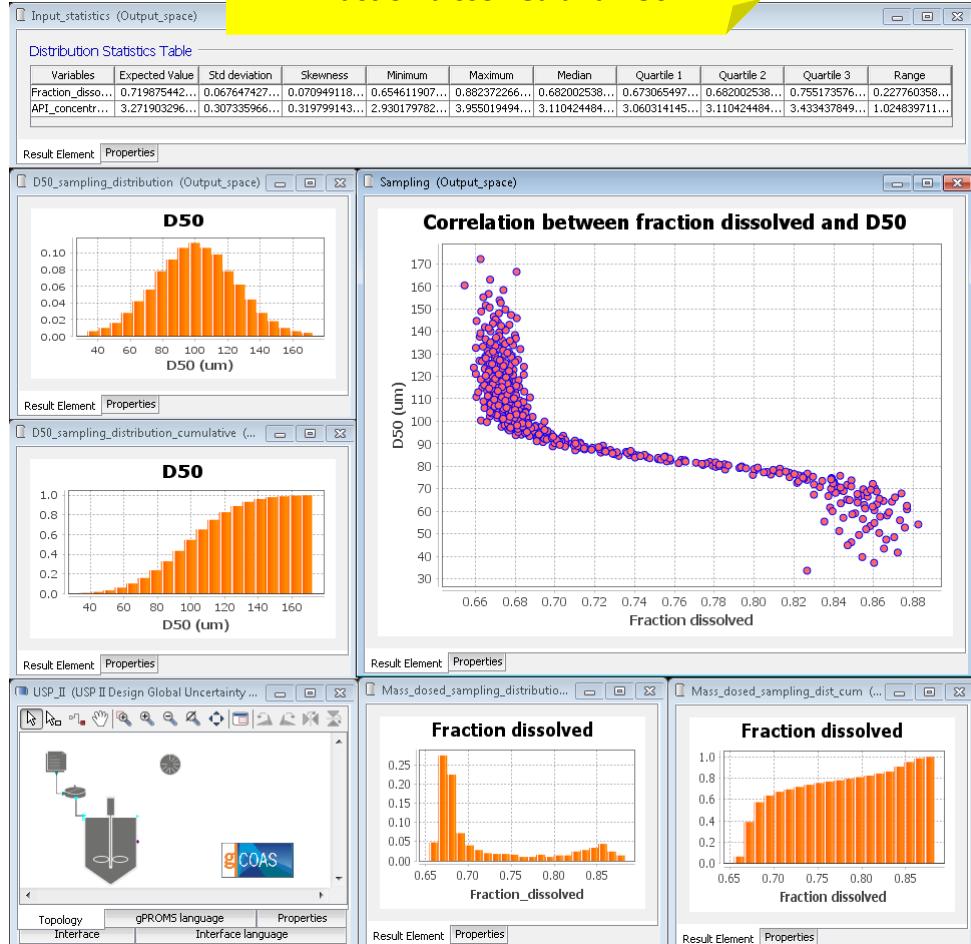


API concentration distribution

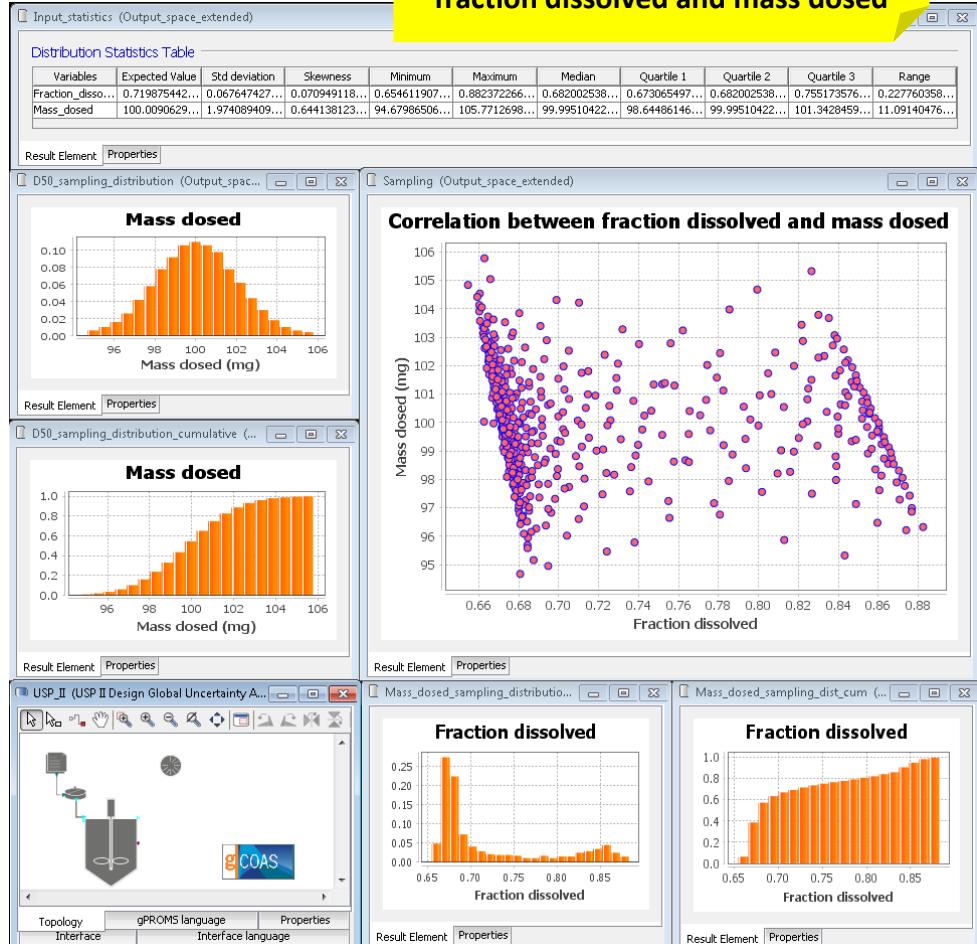
# Global System Analysis in gPROMS

## Results analysis: factor-response correlations

**Correlation between fraction dissolved and D50**

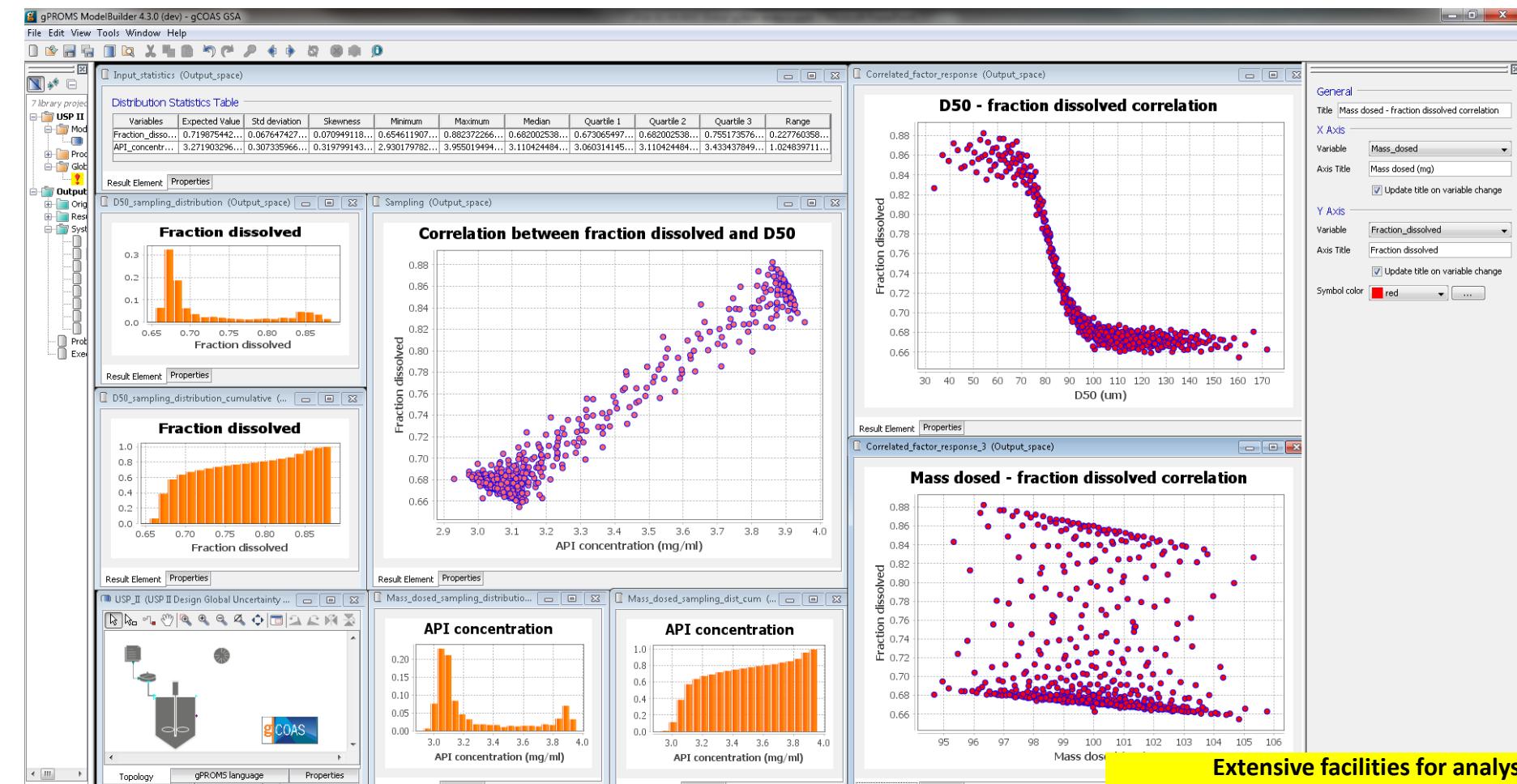


**Correlation between fraction dissolved and mass dosed**



# Global System Analysis in gPROMS

## GSA results management & analysis



Inspect and analyse  
GSA results on the fly

Extensive facilities for analysing  
and presenting large data sets

- System constraints (data filtering),
- Result elements (graphs, tables, images, text etc.)
- Reports associated with such analysis



In conclusion...



## ■ GSA: key to making the most from the modelling investment

- understanding global system behaviour
- quantifying effects of uncertainty
- identifying opportunities for optimisation

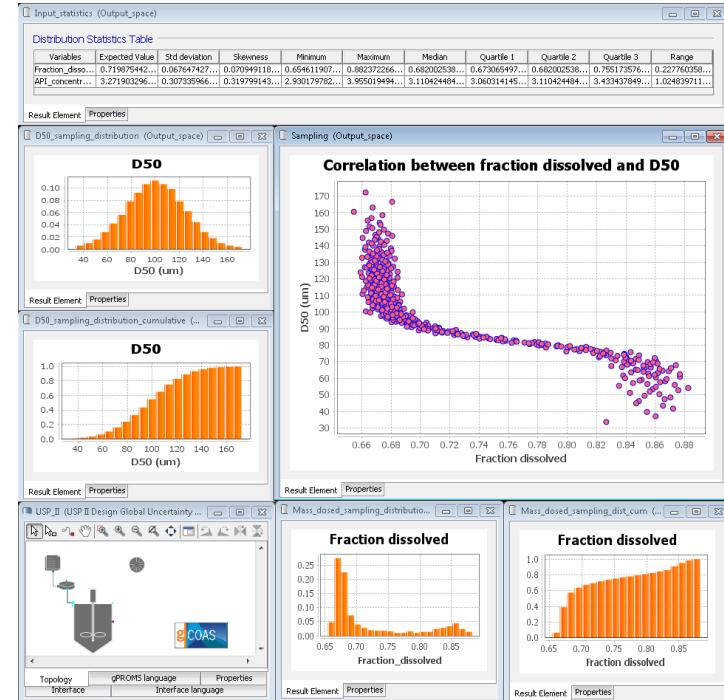
## ■ GSA: tool for investigating model robustness

- identify regions of input space which cause model failure and/or inaccurate predictions

## ■ GSA: major new capability in gPROMS

- ...may become the *main* way in which users interact with models
- ...from a few distinct case studies to full uncertainty/sensitivity analysis

## ■ ...immediately applicable to all gPROMS models

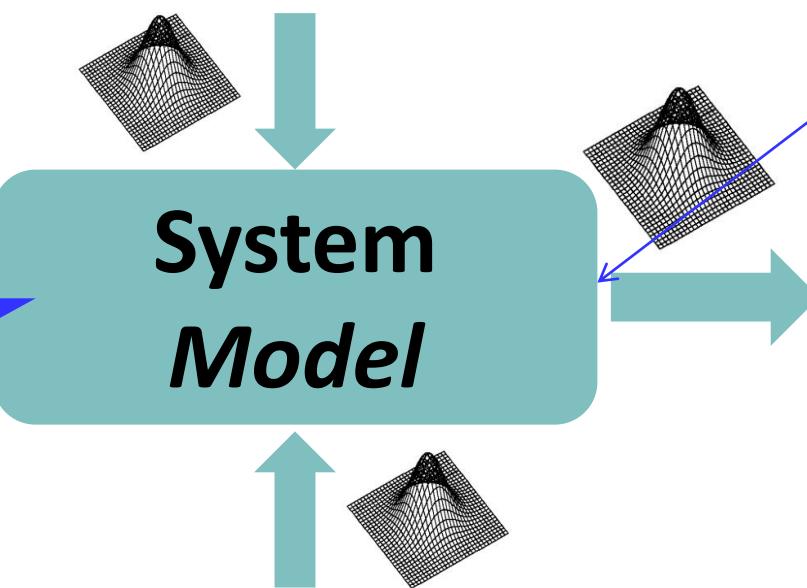


## 2. Reduce variability in environmental inputs

as indicated by Global Sensitivity Indices

### Environmental inputs

- External disturbances
- Commercial environment



## 3. Revise decisions to improve system robustness

Robust Optimisation technology

### Model uncertainty

- Model parameters
- Model structure

## 1. Improve model, reduce parameter uncertainty

R&D focus guided by  
Global Sensitivity Indices

## 4. Modify system

e.g. allow operational  
decisions to be manipulated  
by control system

### KPIs

- Product quality / performance
- Operability
- Safety
- Environmental impact
- Economic performance

Thank you

