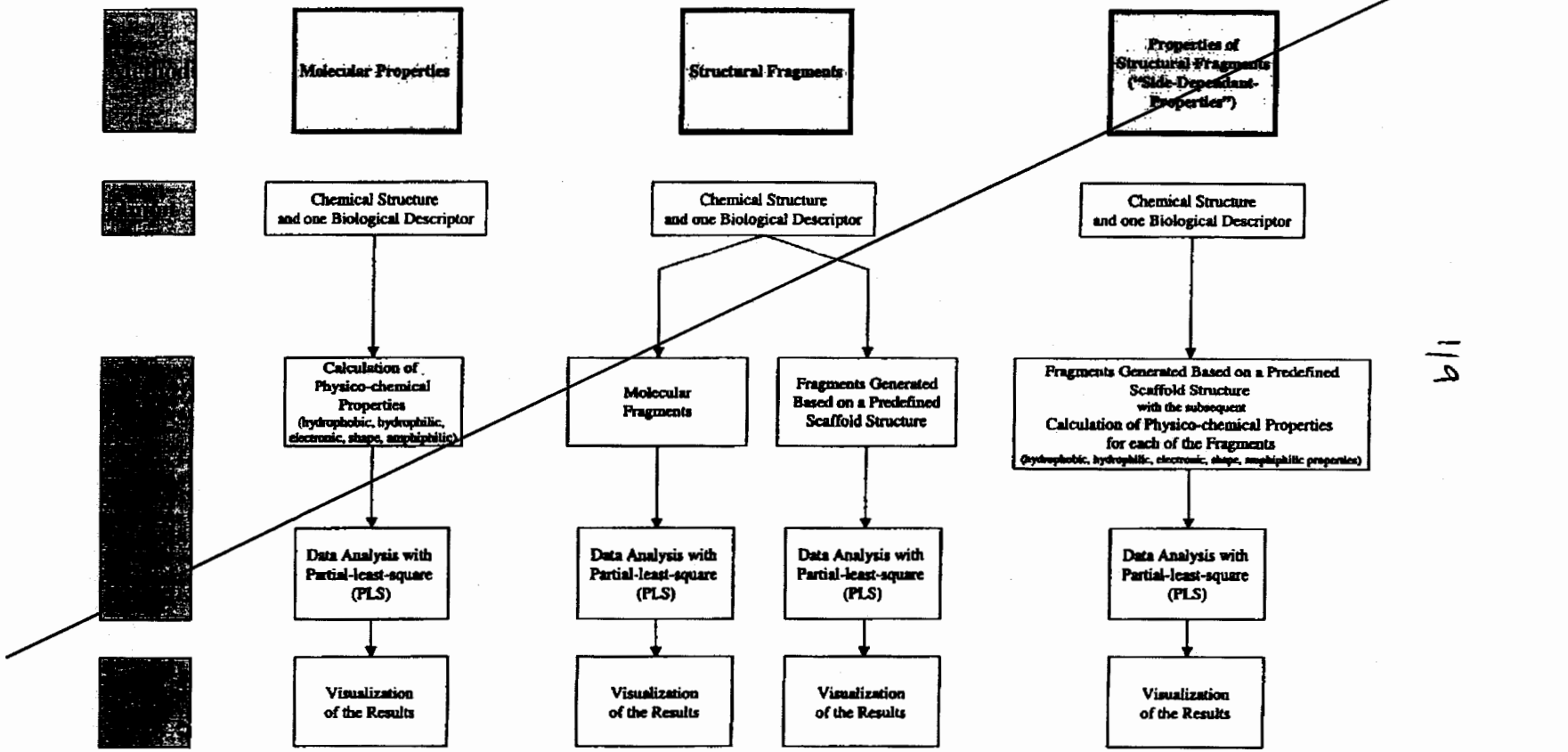
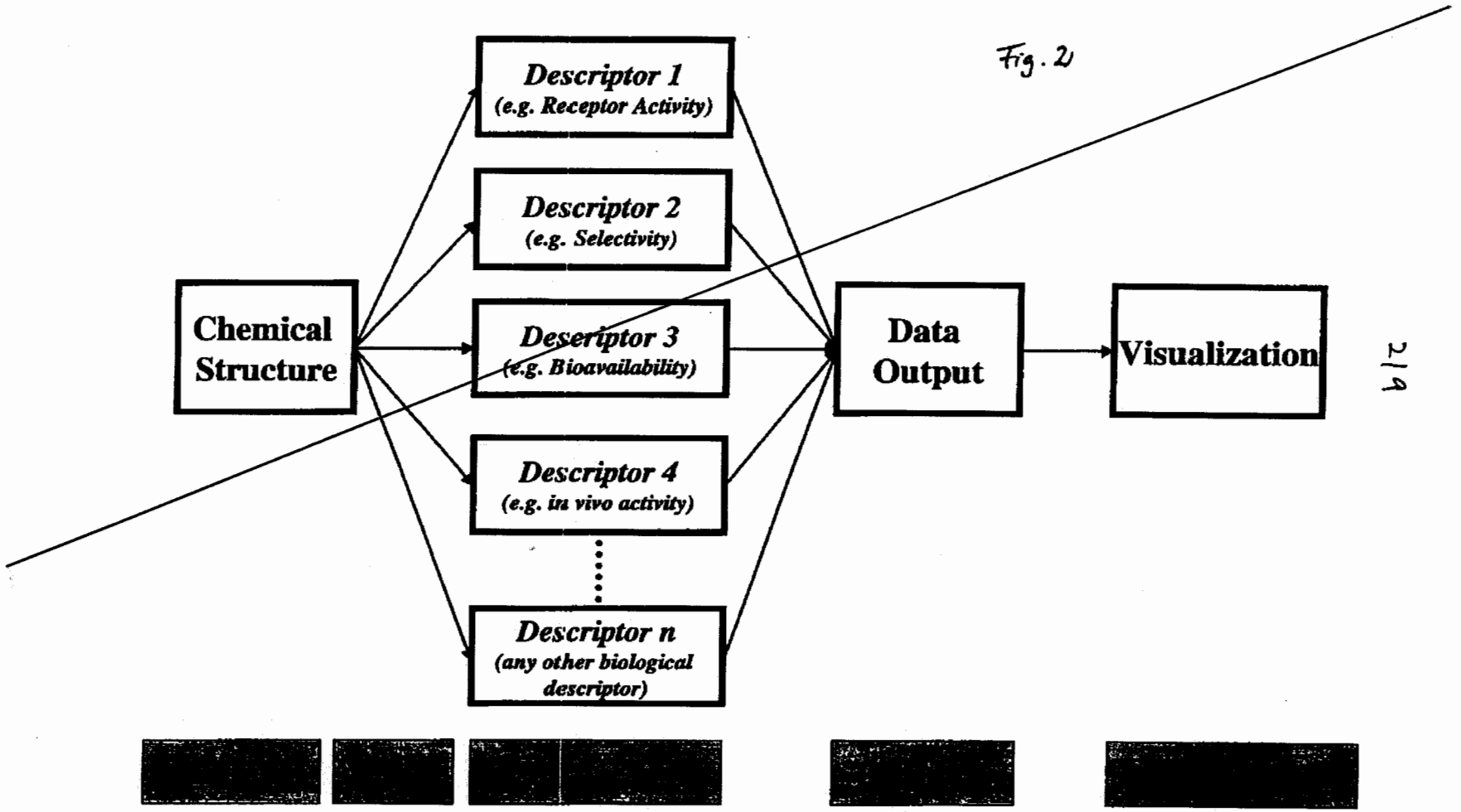

Molecular Properties
Structural Fragments
Properties of Structural Fragments ("Side-Dependant-Properties")
Chemical Structure and one Biological Descriptor
Chemical Structure and one Biological Descriptor
Chemical Structure and one Biological Descriptor
Calculation of Physico-chemical Properties (hydrophobic, hydrophilic, electronic, shape, amphiphilic)
Molecular Fragments
Fragments Generated Based on a Predefined Scaffold Structure
Fragments Generated Based on a Predefined Scaffold Structure with the subsequent Calculation of Physico-chemical Properties for each of the Fragments (hydrophobic, hydrophilic, electronic, shape, amphiphilic properties)
Data Analysis with Partial-least-square (PLS)
Data Analysis with Partial-least-square (PLS)
Data Analysis with Partial-least-square (PLS)
Data Analysis with Partial-least-square (PLS)
Visualization of the Results
Visualization of the Results
Visualization of the Results
Visualization of the Results

Fig. 1

Fig. 2


Descriptor 1
(e.g. Receptor Activity)
Descriptor 2
(e.g. Selectivity)
Chemical Structure
Descriptor 3
(e.g. Bioavailability)
Data Output
Visualization
Descriptor 4
(e.g. in vivo activity)
Descriptor n
(any other biological descriptor)

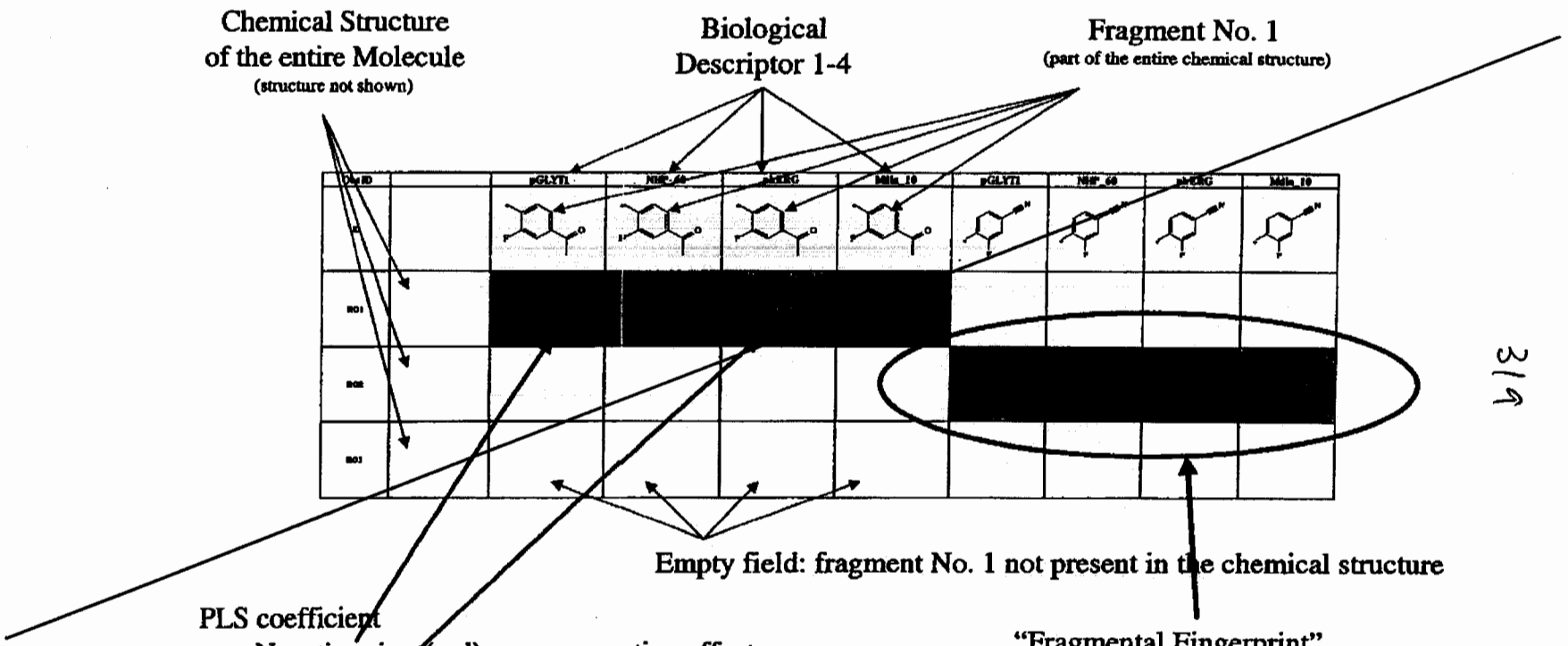

Chemical Structure
of the entire Molecule
(structure not shown)
Biological
Descriptor 1-4
Fragment No. 1
(part of the entire chemical structure)
Empty field: fragment No. 1 not present in the chemical structure
PLS coefficient
- Negative sign (red) means negative effect on biological descriptor (e.g. decrease in biological activity)
- Positive sign (green) means positive effect on biological descriptor (e.g. increase of cardiac safety)
"Fragmental Fingerprint"
(effect of one fragment on a "whole" biological profile comparable with a genetic fingerprint)

Fig. 3

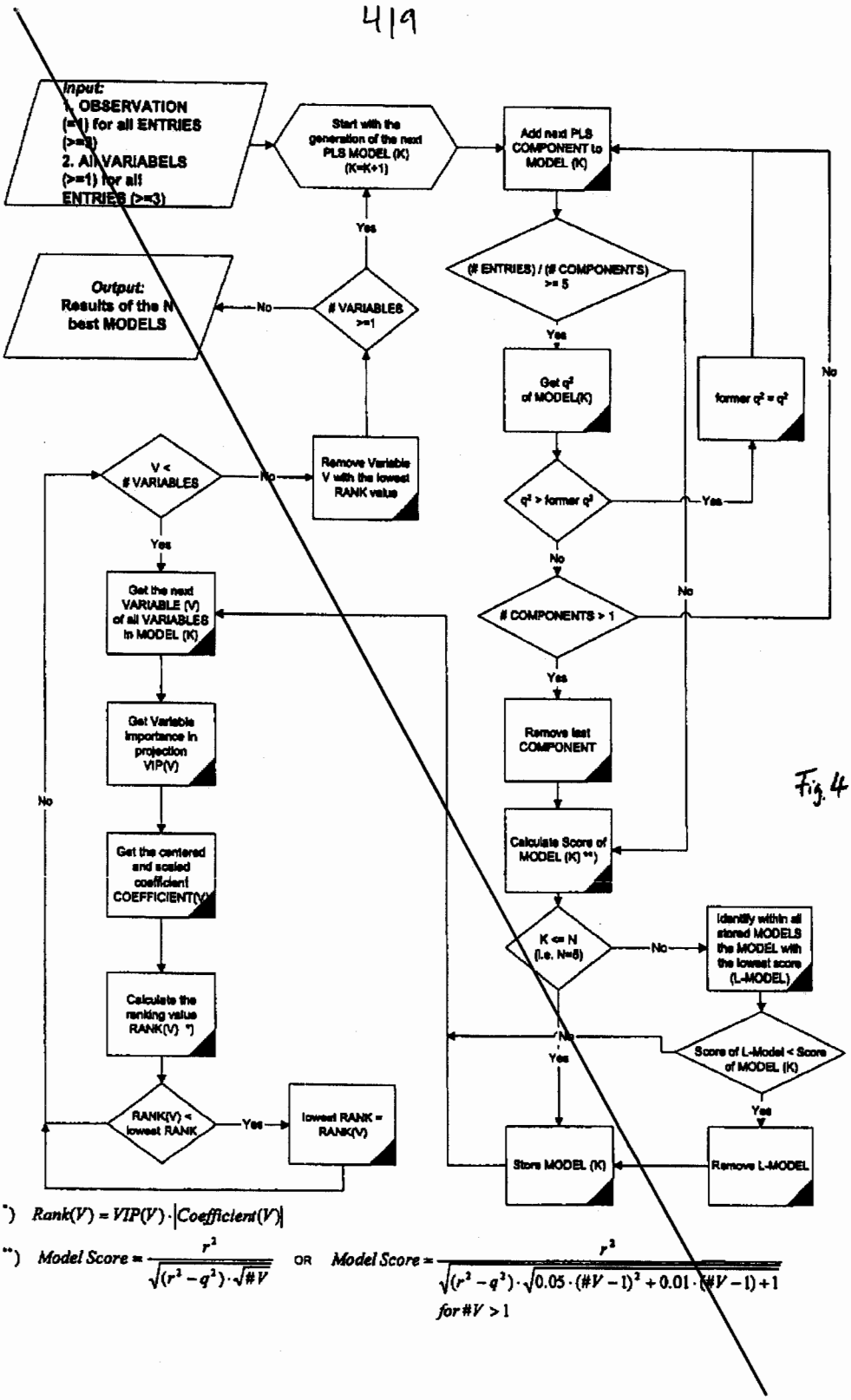
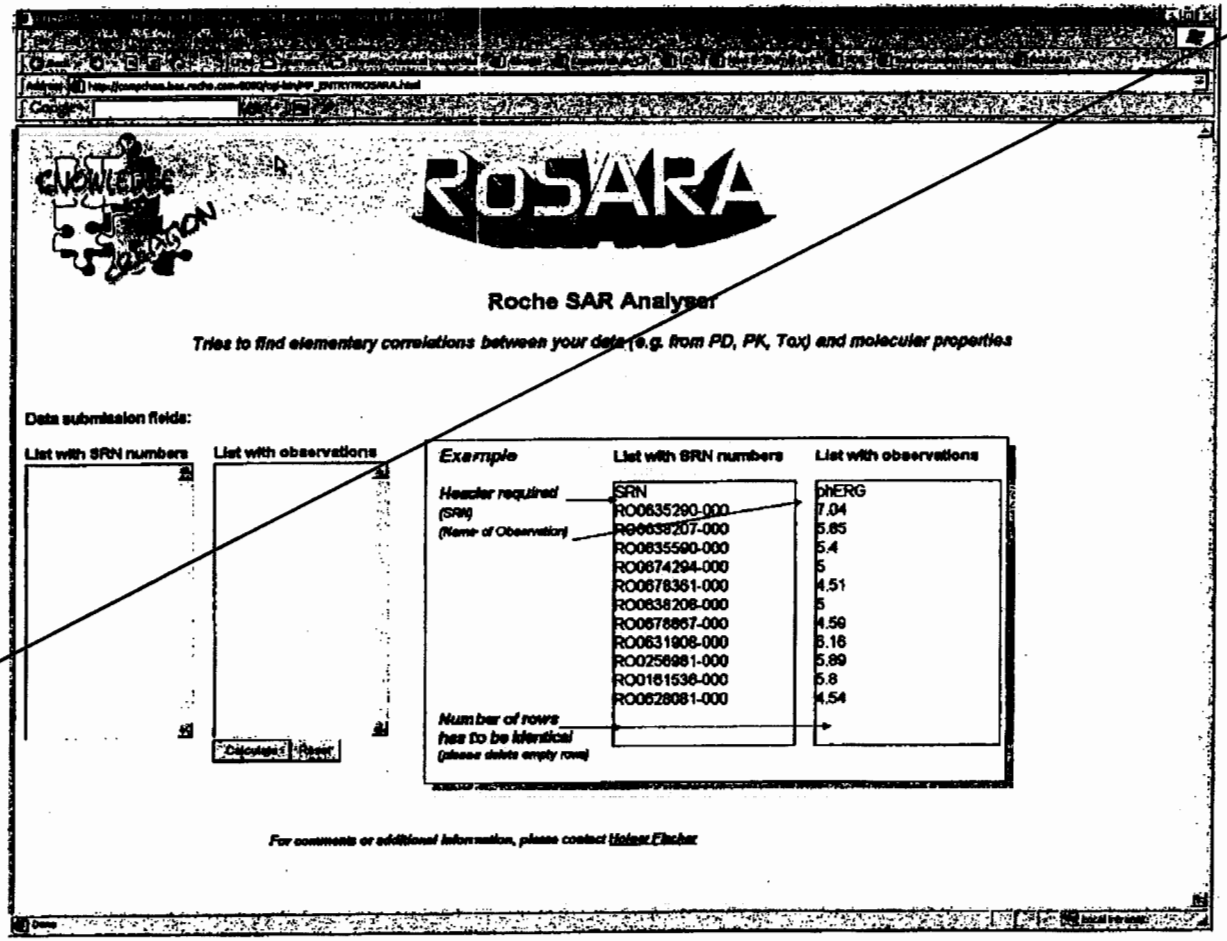


Fig. 4

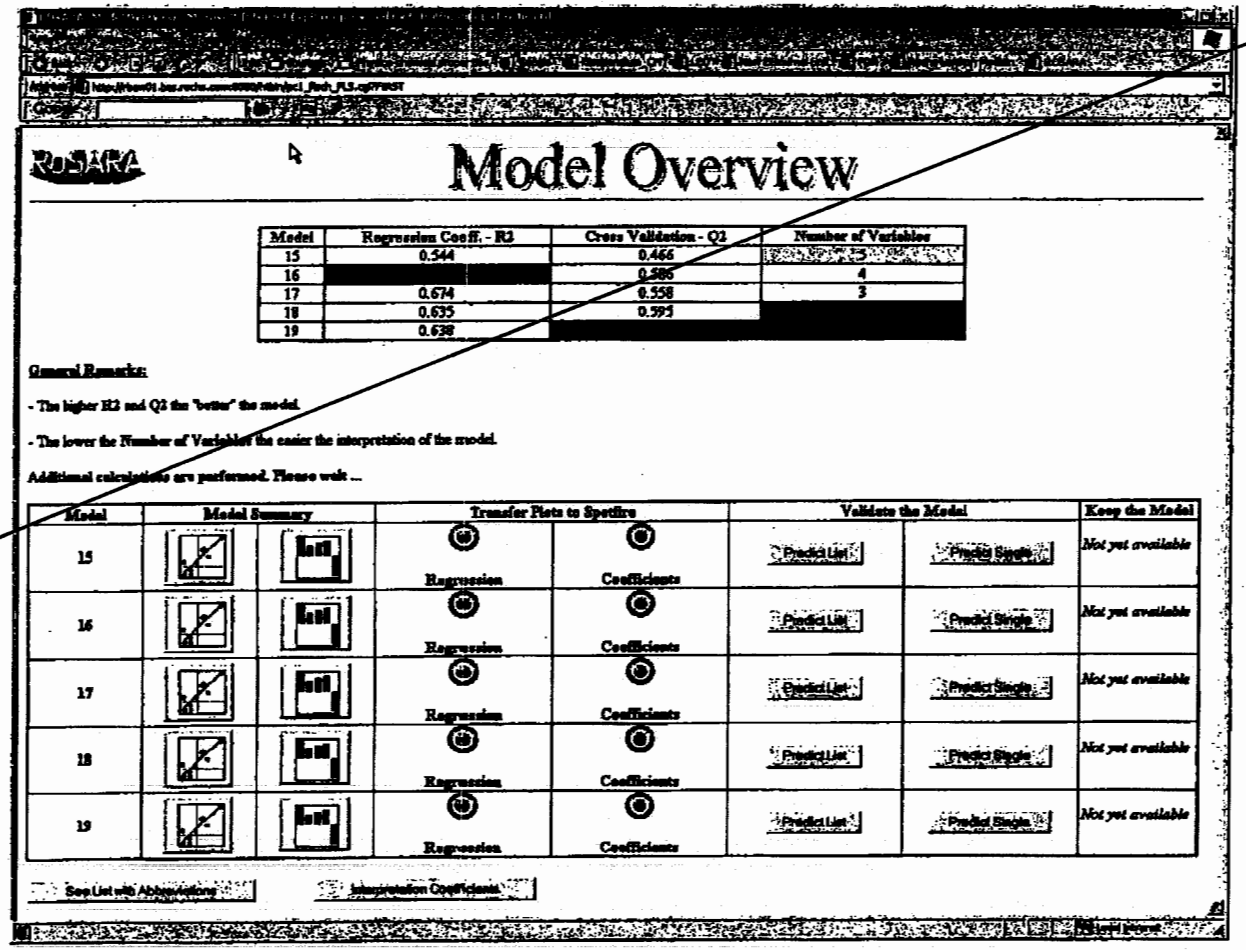
*) $Rank(V) = VIP(V) \cdot |Coefficient(V)|$

**) $Model\ Score = \frac{r^2}{\sqrt{(r^2 - q^2) \cdot \sqrt{\#V}}}$ OR $Model\ Score = \frac{r^2}{\sqrt{(r^2 - q^2) \cdot \sqrt{0.05 \cdot (\#V - 1)^2 + 0.01 \cdot (\#V - 1) + 1}}}$ for $\#V > 1$


ROSARA
Roche SAR Analyser
Tries to find elementary correlations between your data (e.g. from PD, PK, Tox) and molecular properties
Data submission fields:
List with SRN numbers
List with observations
Example
List with SRN numbers
List with observations
Header required
(SRN)
(Name of Observation)
SRN
phERG
RO0635290-000
7.04
RO0638207-000
5.85
RO0635590-000
5.4
RO0674294-000
5
RO0678361-000
4.51
RO0638206-000
5
RO0678667-000
4.59
RO0631908-000
5.16
RO0256981-000
5.89
RO0161536-000
5.8
RO0628081-000
4.54
Number of rows
has to be identical
(please delete empty rows)
For comments or additional information, please contact Holger Fischer

519

Fig 5


ROSAIRA
Model Overview
Model | Regression Coeff. - R2 | Cross Validation - Q2 | Number of Variables
15 | 0.544 | 0.466 |
16 | | 0.586 | 4
17 | 0.674 | 0.558 | 3
18 | 0.635 | 0.595 |
19 | 0.638 |
General Remarks:
- The higher R2 and Q2 the "better" the model.
- The lower the Number of Variables the easier the interpretation of the model.
Additional calculations are performed. Please wait ...
Model | Model Summary | Transfer Plots to Spotfire | Validate the Model | Keep the Model
15 | Regression | Coefficients | Predict List | Predict Single | Not yet available
16 | Regression | Coefficients | Predict List | Predict Single | Not yet available
17 | Regression | Coefficients | Predict List | Predict Single | Not yet available
18 | Regression | Coefficients | Predict List | Predict Single | Not yet available
19 | Regression | Coefficients | Predict List | Predict Single | Not yet available
Step List with Abbreviations
Interpretation Coefficients

619

Fig 6

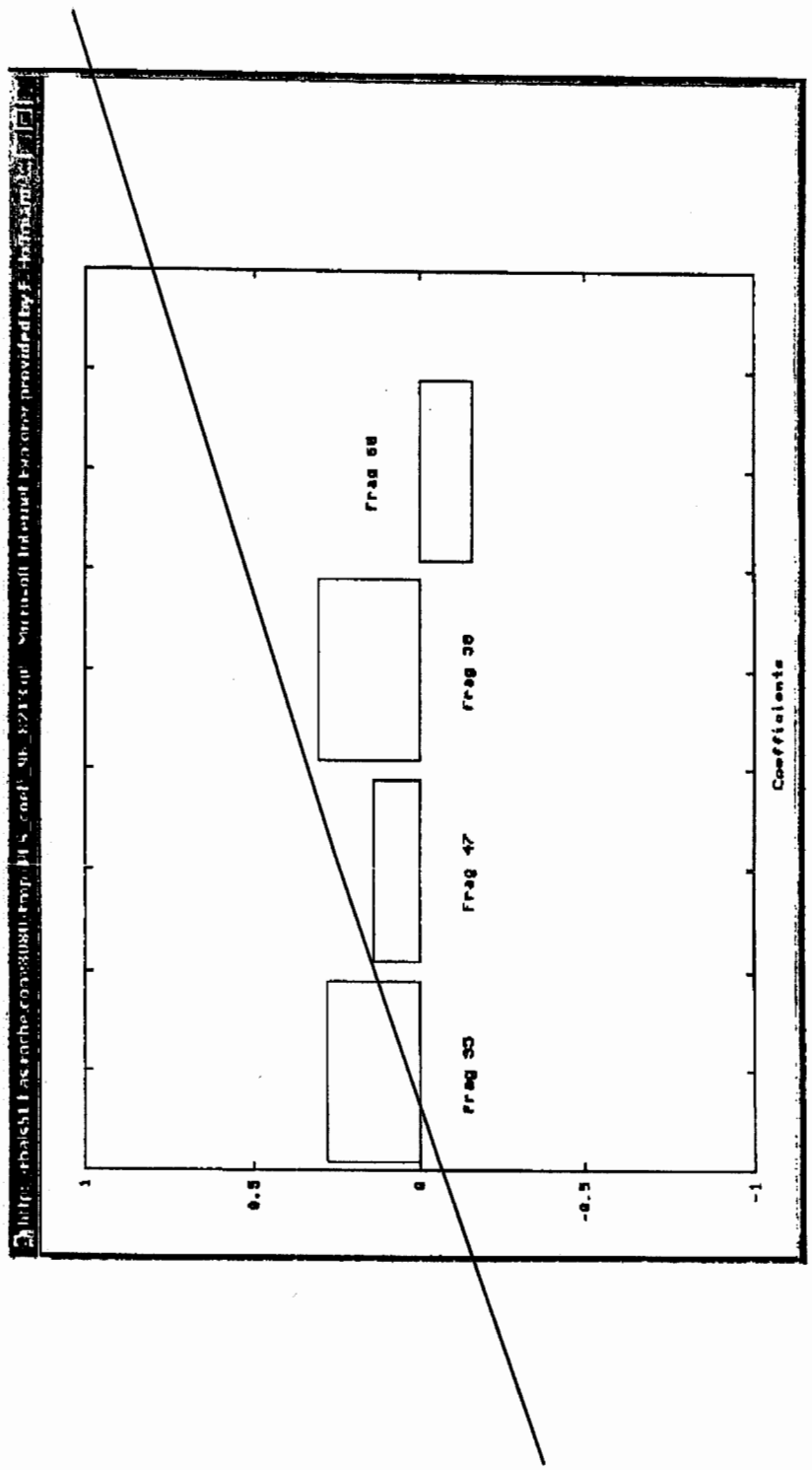


Fig. 7

819

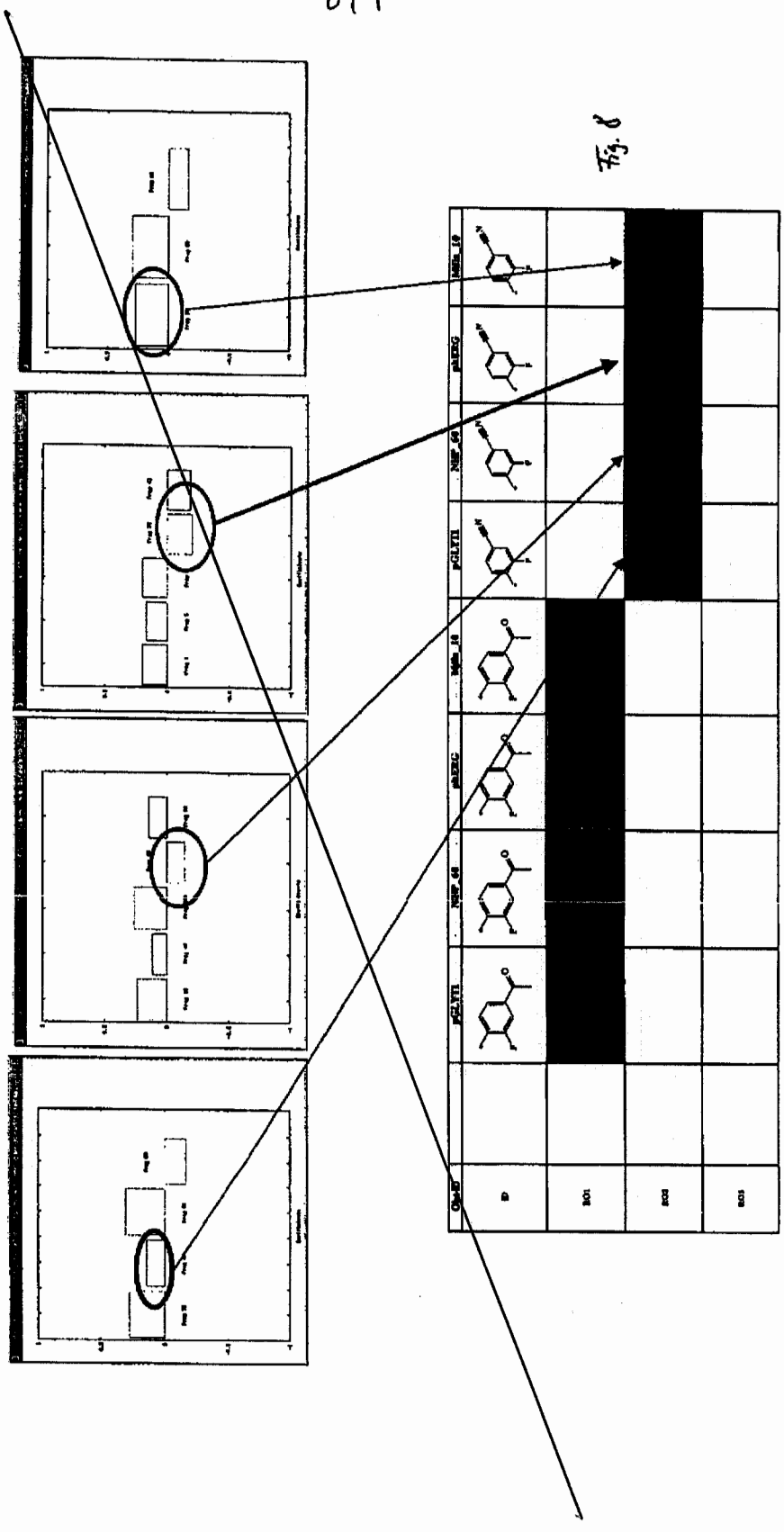


Fig. 8

Structure	pGLYT1	NHP_60	phERG	Mdla_1(
Chemistry 12	[redacted]			
Chemistry 13				
Chemistry 14				
Chemistry 15				
Chemistry 16				
Chemistry 17				
Chemistry 21				
Chemistry 22				
Chemistry 23				
Chemistry 41				
Chemistry 42				
Chemistry 43				
Chemistry 27				
Chemistry 28				
Chemistry 29				
Chemistry 30				
Chemistry 31				
Chemistry 32				
Chemistry 38				
Chemistry 39				
Chemistry 40				

Fig. 9

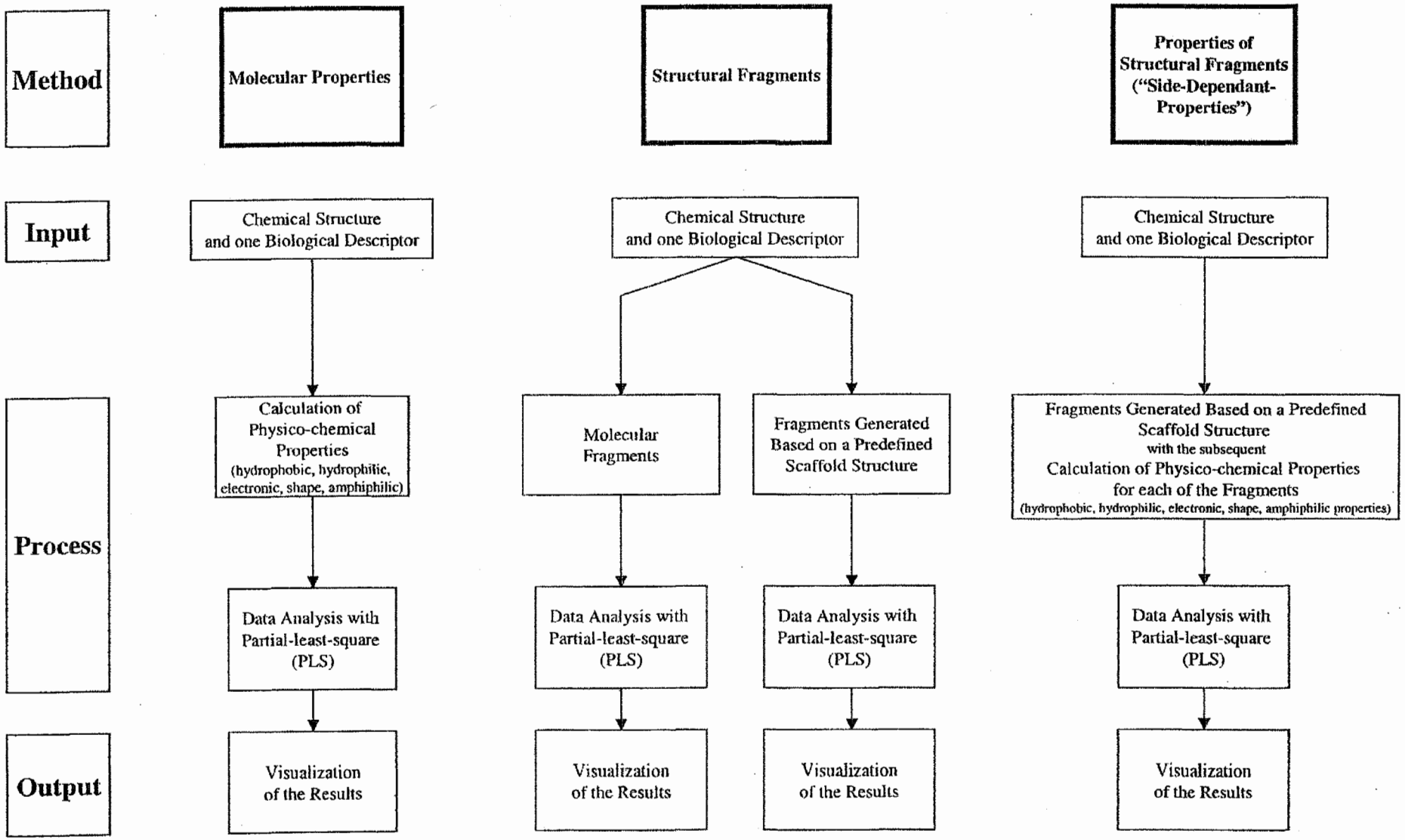
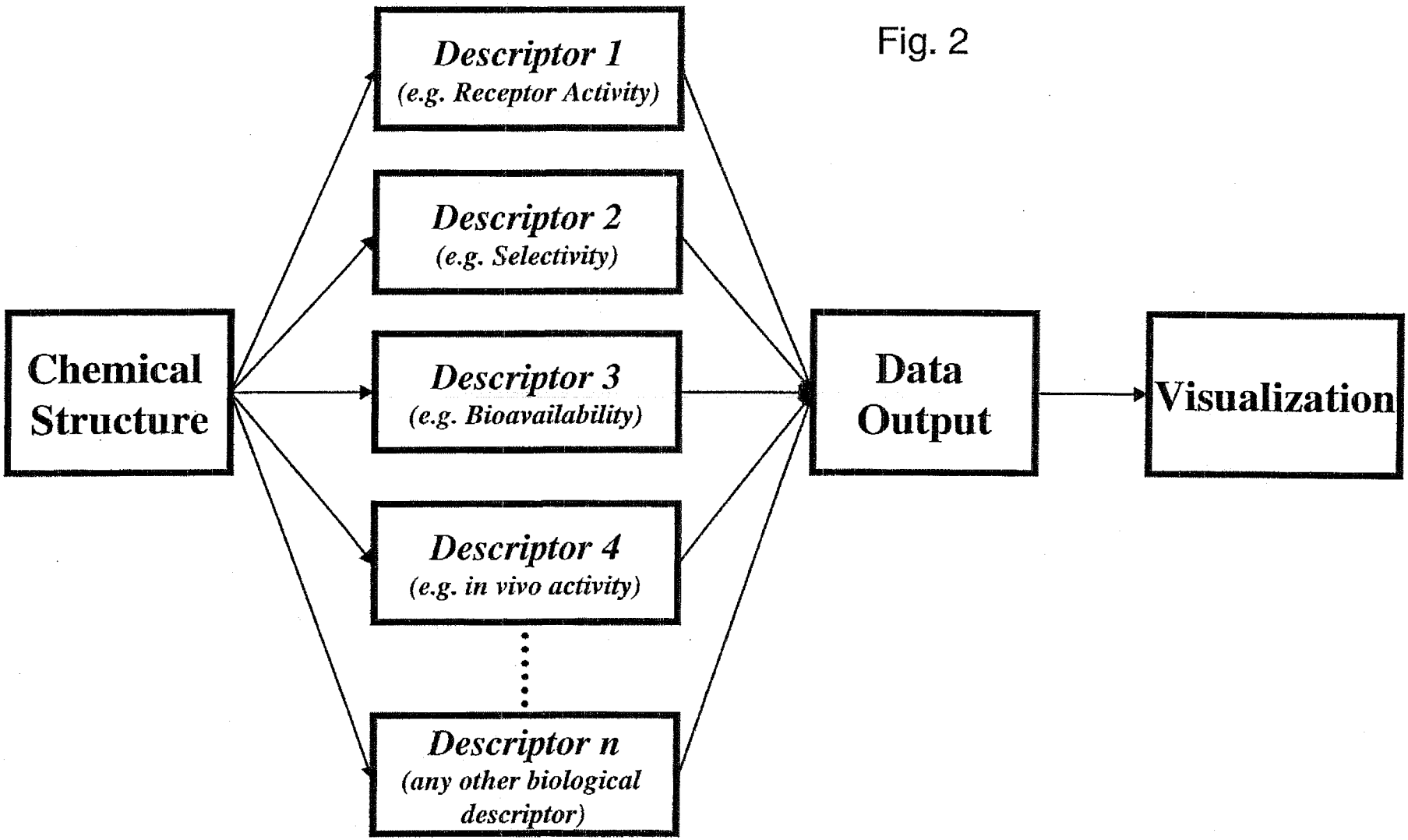

Method
Molecular Properties
Structural Fragments
Properties of Structural Fragments ("Side-Dependant-Properties")
Input
Chemical Structure and one Biological Descriptor
Chemical Structure and one Biological Descriptor
Chemical Structure and one Biological Descriptor
Process
Calculation of Physico-chemical Properties (hydrophobic, hydrophilic, electronic, shape, amphiphilic)
Molecular Fragments
Fragments Generated Based on a Predefined Scaffold Structure
Fragments Generated Based on a Predefined Scaffold Structure with the subsequent Calculation of Physico-chemical Properties for each of the Fragments (hydrophobic, hydrophilic, electronic, shape, amphiphilic properties)
Data Analysis with Partial-least-square (PLS)
Data Analysis with Partial-least-square (PLS)
Data Analysis with Partial-least-square (PLS)
Data Analysis with Partial-least-square (PLS)
Output
Visualization of the Results
Visualization of the Results
Visualization of the Results
Visualization of the Results

Fig. 1

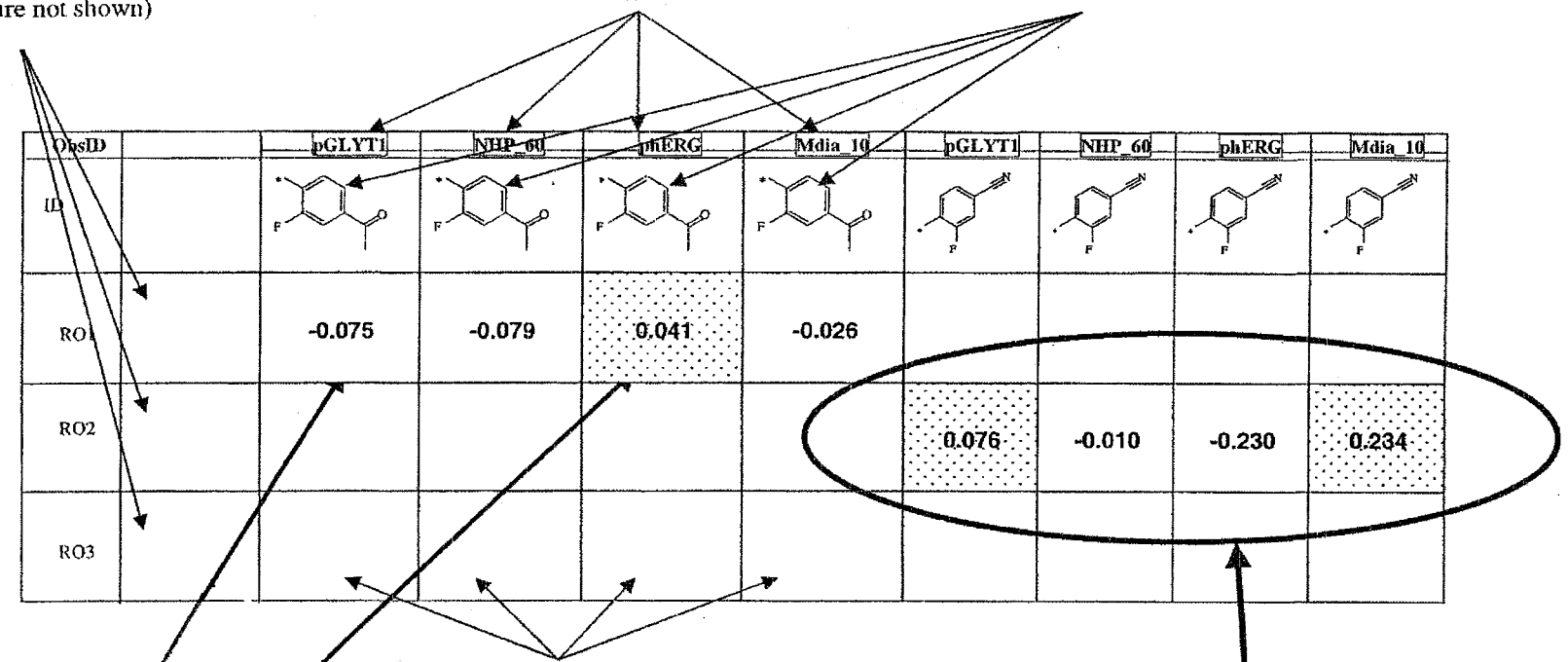
Fig. 2


Descriptor 1
(e.g. Receptor Activity)
Descriptor 2
(e.g. Selectivity)
Descriptor 3
(e.g. Bioavailability)
Descriptor 4
(e.g. in vivo activity)
Descriptor n
(any other biological descriptor)
Chemical Structure
Data Output
Visualization
Input
Method
Process
Output
Visualization

Chemical Structure
of the entire Molecule
(structure not shown)

Biological
Descriptor 1-4

Fragment No. 1
(part of the entire chemical structure)



Empty field: fragment No. 1 not present in the chemical structure

PLS coefficient

- Negative sign (red) means negative effect on biological descriptor (e.g. decrease in biological activity)
- Positive sign (green) means positive effect on biological descriptor (e.g. increase of cardiac safety)

"Fragmental Fingerprint"
(effect of one fragment on a "whole" biological profile comparable with a genetic fingerprint)

Fig. 3

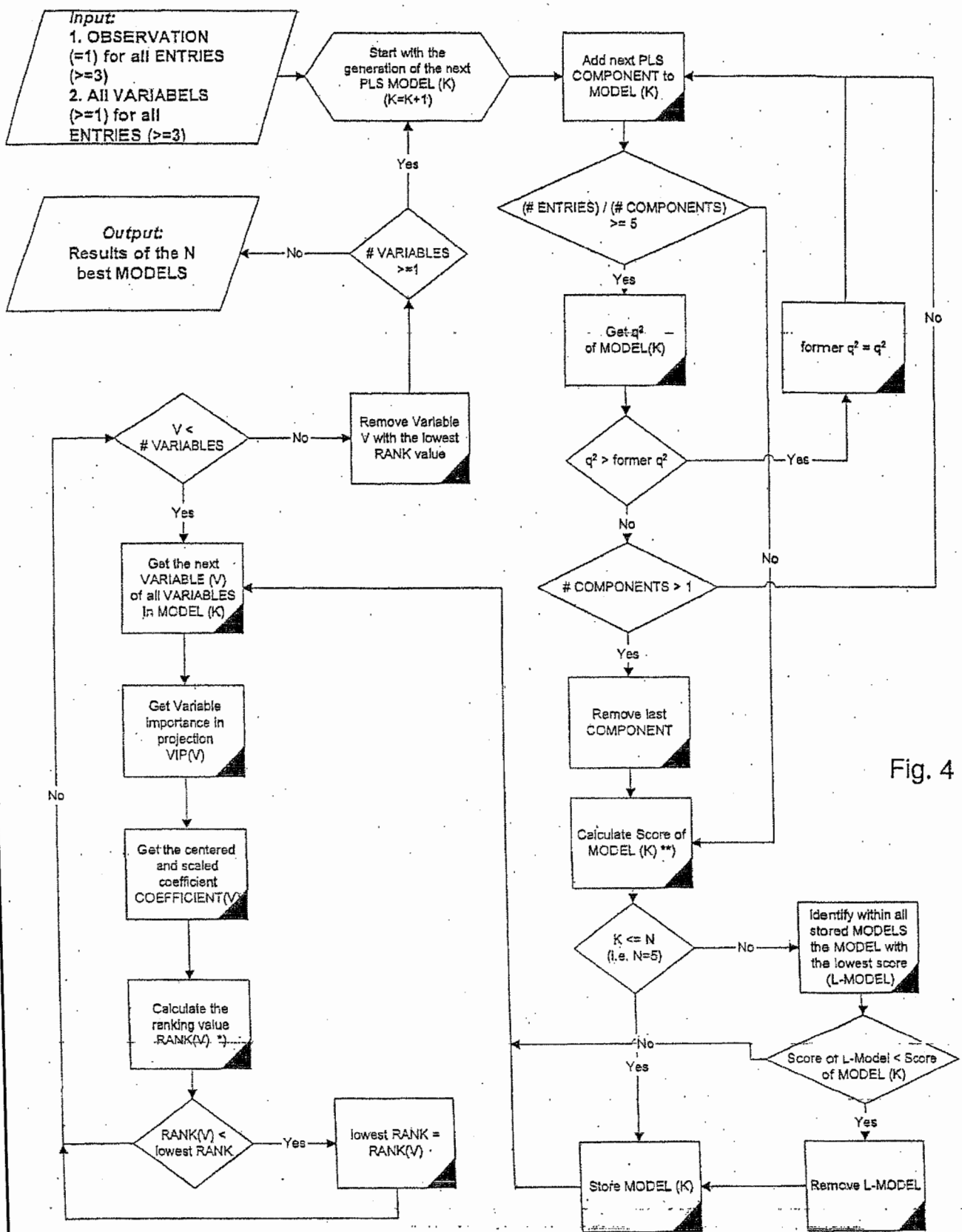


Fig. 4

*) $Rank(V) = VIP(V) \cdot |Coefficient(V)|$

**) $Model\ Score = \frac{r^2}{\sqrt{(r^2 - q^2) \cdot \sqrt{\#V}}}$ OR $Model\ Score = \frac{r^2}{\sqrt{(r^2 - q^2) \cdot \sqrt{0.05 \cdot (\#V - 1)^2 + 0.01 \cdot (\#V - 1) + 1}}}$ $for\ \#V > 1$

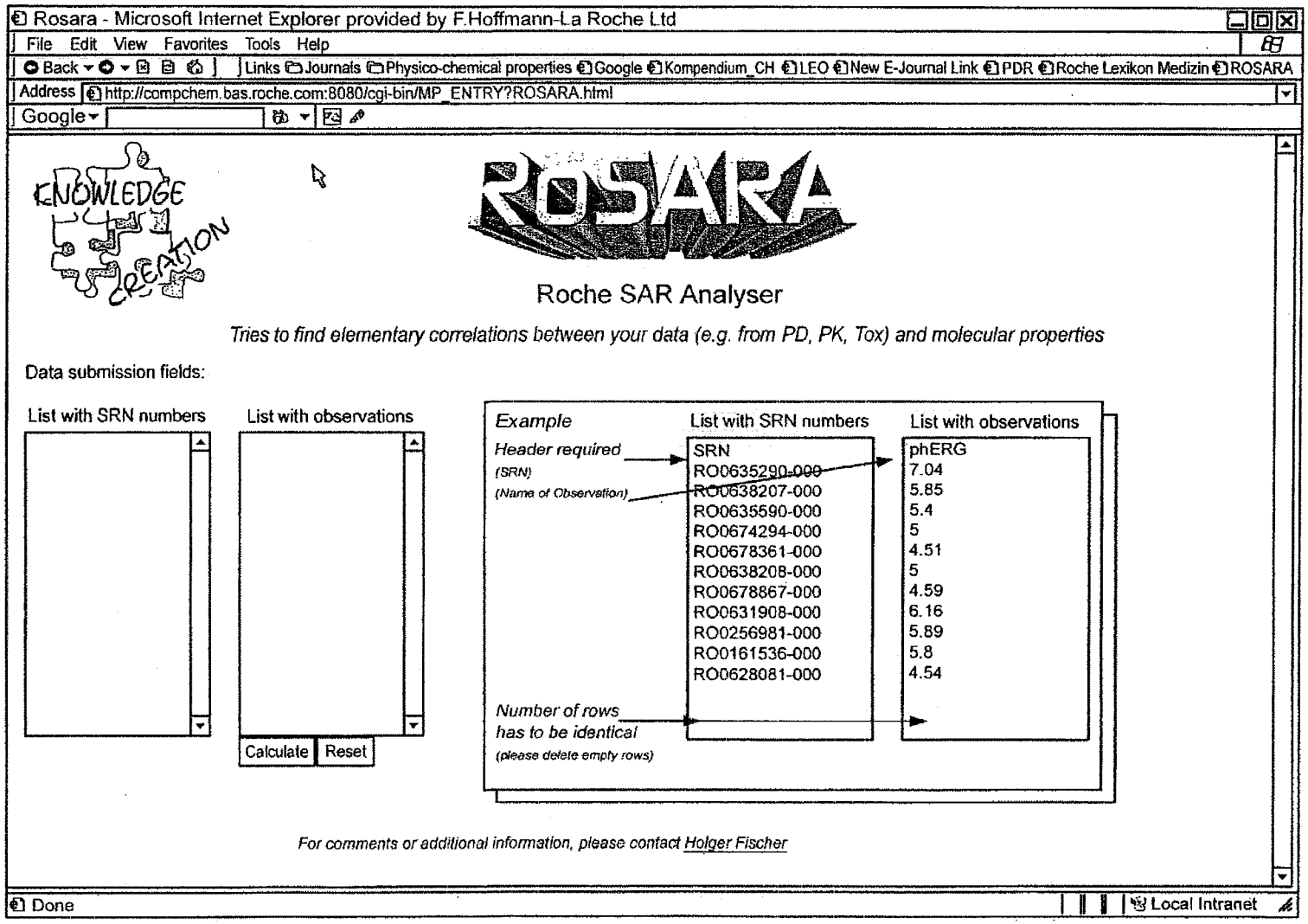

Rosara - Microsoft Internet Explorer provided by F.Hoffmann-La Roche Ltd
File Edit View Favorites Tools Help
Back
Links Journals Physico-chemical properties Google Kompendium_CH LEO New E-Journal Link PDR Roche Lexikon Medizin ROSARA
Address http://compchem.bas.roche.com:8080/cgi-bin/MP_ENTRY?ROSARA.html
Google
KNOWLEDGE CREATION
ROSARA
Roche SAR Analyser
Tries to find elementary correlations between your data (e.g. from PD, PK, Tox) and molecular properties
Data submission fields:
List with SRN numbers
List with observations
Calculate
Reset
Example
List with SRN numbers
List with observations
Header required
(SRN)
(Name of Observation)
SRN
RO0635290-000
RO0638207-000
RO0635590-000
RO0674294-000
RO0678361-000
RO0638208-000
RO0678867-000
RO0631908-000
RO0256981-000
RO0161536-000
RO0628081-000
phERG
7.04
5.85
5.4
5
4.51
5
4.59
6.16
5.89
5.8
4.54
Number of rows has to be identical
(please delete empty rows)
For comments or additional information, please contact Holger Fischer
Done
Local Intranet

Fig. 5

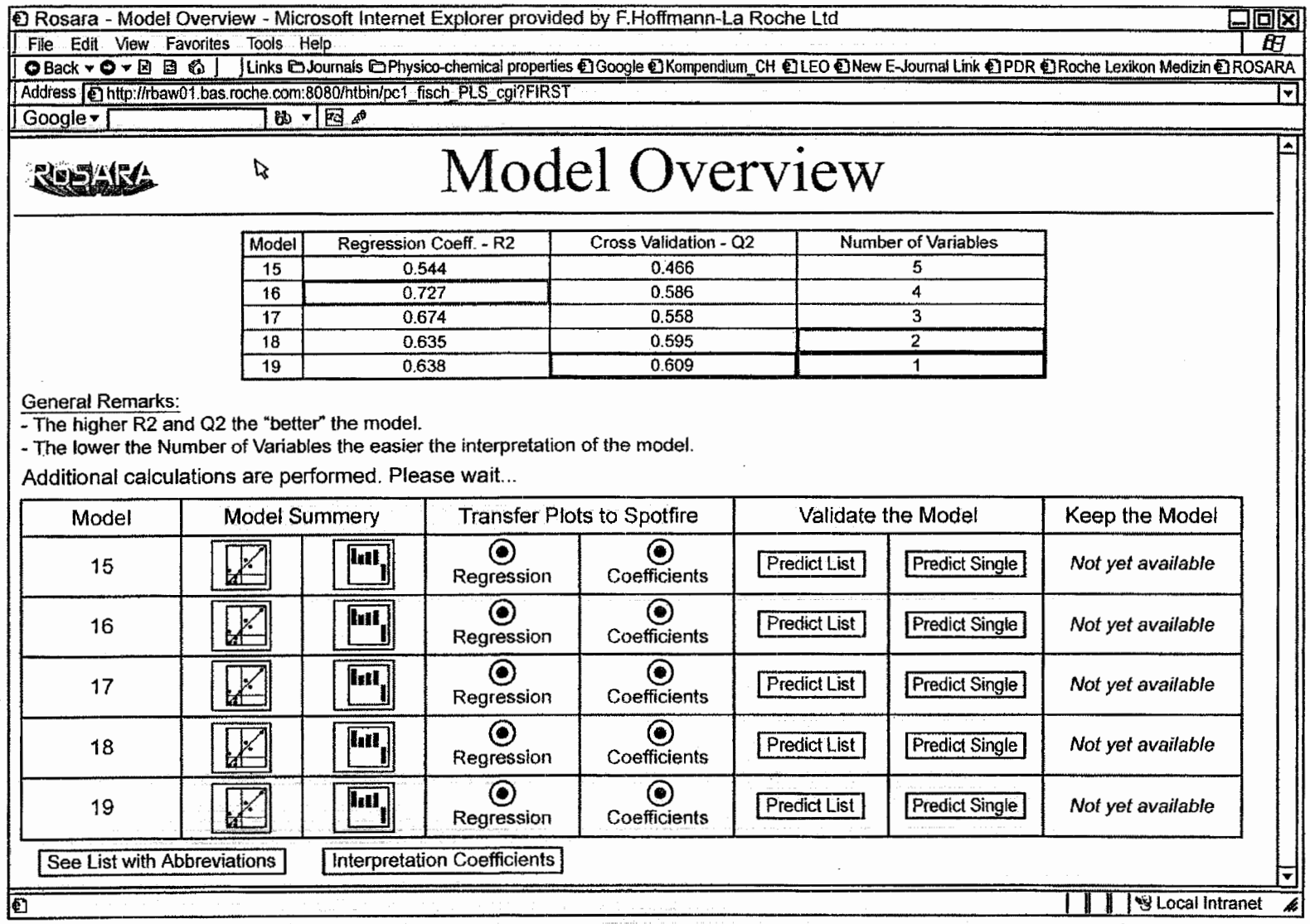

Rosara - Model Overview - Microsoft Internet Explorer provided by F.Hoffmann-La Roche Ltd
File Edit View Favorites Tools Help
Back
Links Journals Physico-chemical properties Google Kompendium_CH LEO New E-Journal Link PDR Roche Lexikon Medizin ROSARA
Address http://rbaw01.bas.roche.com:8080/htbin/pc1_fisch_PLS_cgi?FIRST
Google
ROSARA
Model Overview
Model | Regression Coeff. - R2 | Cross Validation - Q2 | Number of Variables
15 | 0.544 | 0.466 | 5
16 | 0.727 | 0.586 | 4
17 | 0.674 | 0.558 | 3
18 | 0.635 | 0.595 | 2
19 | 0.638 | 0.609 | 1
General Remarks:
- The higher R2 and Q2 the "better" the model.
- The lower the Number of Variables the easier the interpretation of the model.
Additional calculations are performed. Please wait...
Model | Model Summery | Transfer Plots to Spotfire | Validate the Model | Keep the Model
15 | Regression | Coefficients | Predict List | Predict Single | Not yet available
16 | Regression | Coefficients | Predict List | Predict Single | Not yet available
17 | Regression | Coefficients | Predict List | Predict Single | Not yet available
18 | Regression | Coefficients | Predict List | Predict Single | Not yet available
19 | Regression | Coefficients | Predict List | Predict Single | Not yet available
See List with Abbreviations
Interpretation Coefficients
Local Intranet

Fig. 6

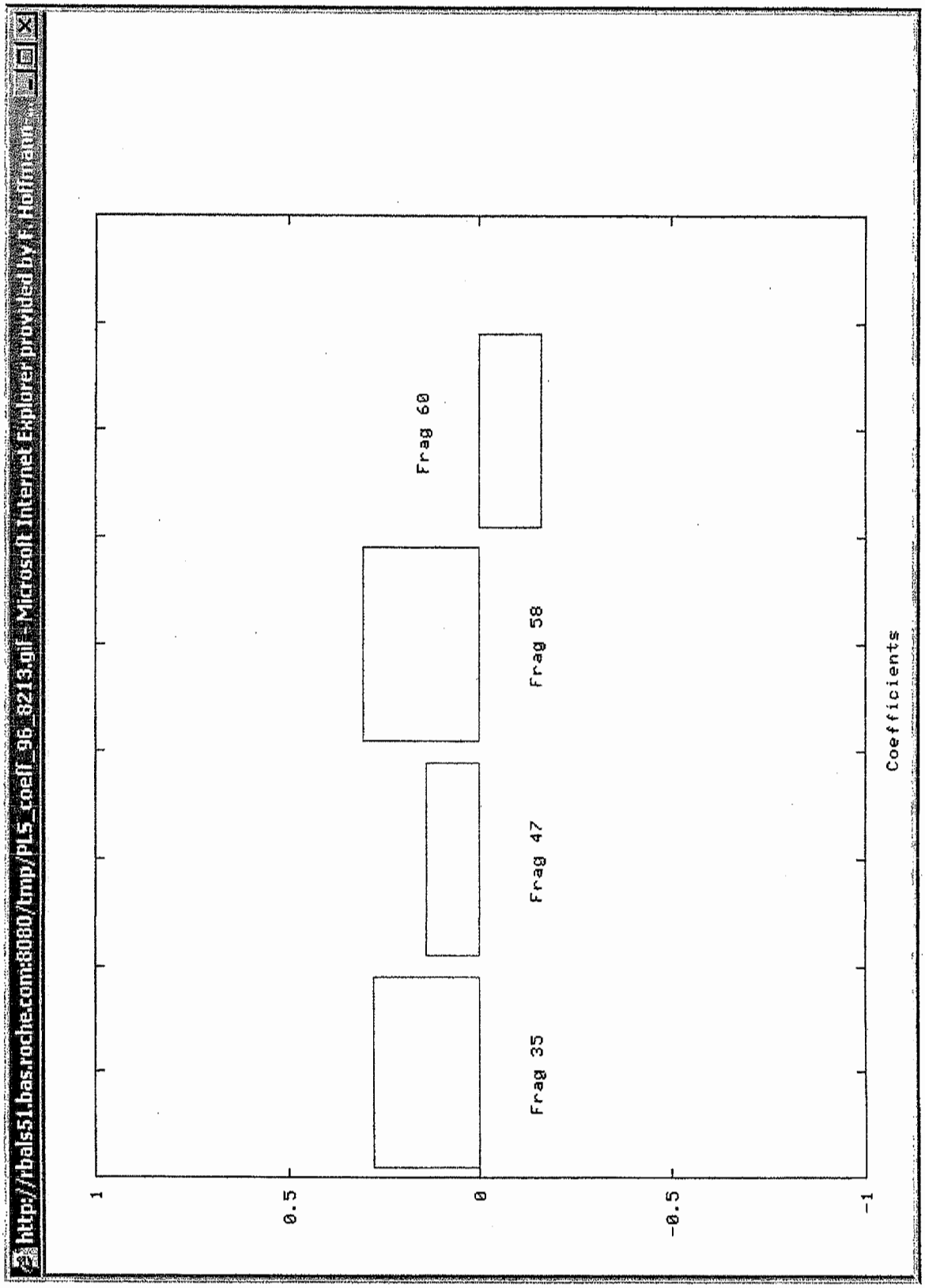

http://rbals51.bas.roche.com:8080/tmp/PLS_coeff_96_8213.gif - Microsoft Internet Explorer provided by F. Hoffmann
1
0.5
0
-0.5
-1
Frag 35
Frag 47
Frag 58
Frag 60
Coefficients

Fig. 7

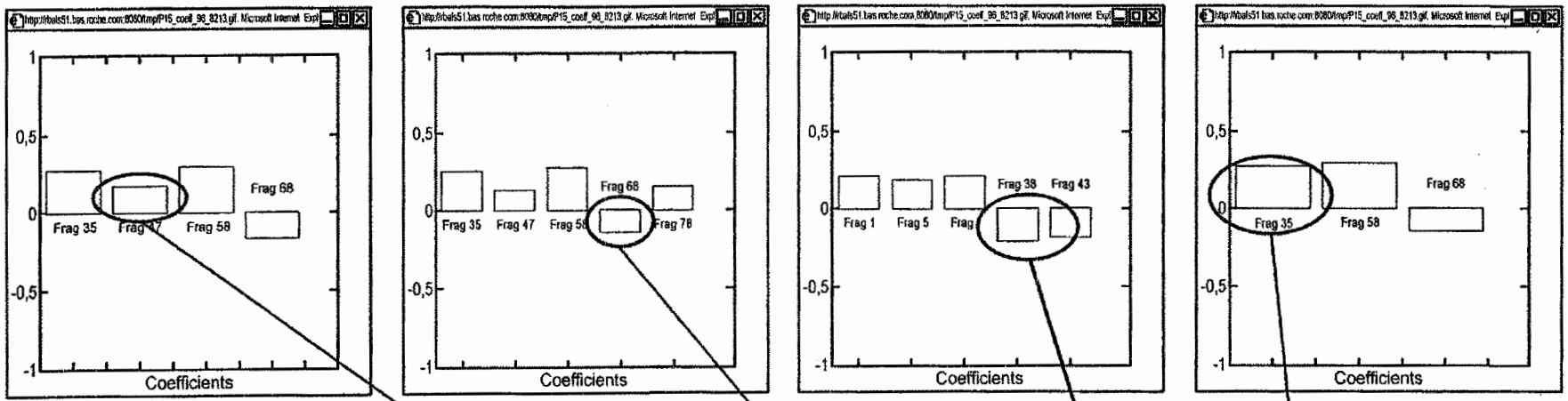
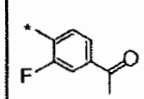
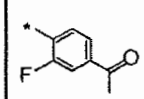
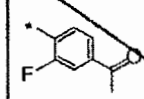
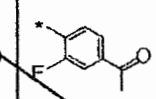
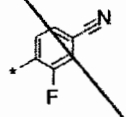
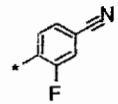
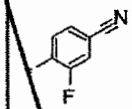
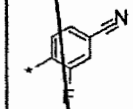


Fig. 8

ObsID		pGLYT1	NHP_60	phERG	Mdia_10	pGLYT1	NHP_60	phERG	Mdia_10
ID									
RO1		-0.075	-0.079	0.041	-0.026				
RO2						0.076	-0.010	-0.230	0.234
RO3									

Structure	pGLYT1	NHP_60	phERG	Mdia_10	Ranking Score
Chemistry 12	0.222	0.14	0.126	0.122	0.528
Chemistry 13	0.222	0.14	0.126	0.122	0.528
Chemistry 14	0.222	0.14	0.126	0.122	0.528
Chemistry 15	0.18	0.132	0.107	0.143	0.514
Chemistry 16	0.18	0.132	0.107	0.143	0.514
Chemistry 17	0.18	0.132	0.107	0.143	0.514
Chemistry 21	0.192	0.15	0.054	0.134	0.488
Chemistry 22	0.192	0.15	0.054	0.134	0.488
Chemistry 23	0.192	0.15	0.054	0.134	0.488
Chemistry 41	0.074	0.121	0.072	0.169	0.483
Chemistry 42	0.074	0.121	0.072	0.169	0.483
Chemistry 43	0.074	0.121	0.072	0.169	0.483
Chemistry 27	0.15	0.142	0.035	0.155	0.474
Chemistry 28	0.15	0.142	0.035	0.155	0.474
Chemistry 29	0.15	0.142	0.035	0.155	0.474
Chemistry 30	0.118	0.112	0.077	0.171	0.472
Chemistry 31	0.118	0.112	0.077	0.171	0.472
Chemistry 32	0.118	0.112	0.077	0.171	0.472
Chemistry 38	0.069	0.096	0.112	0.162	0.466
Chemistry 39	0.069	0.096	0.112	0.162	0.466
Chemistry 40	0.069	0.096	0.112	0.162	0.466

Fig. 9