

# **“INTEGRATED CONCEPT” for INSILICO SCREENING & DRUG DESIGN**

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**ACTIVITY, ADME, TOXICITY, PROPERTY  
ANALYSIS AND PREDICTION**

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In Silico Data, Ltd.

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*“Integrated” concept*

2

*Application pattern of integrated concept*

*“Integrated in silico screening”*

*“Integrated in silico drug design”*

3

*Multivariate and pattern recognition*

**From pattern analysis to scientific analysis**

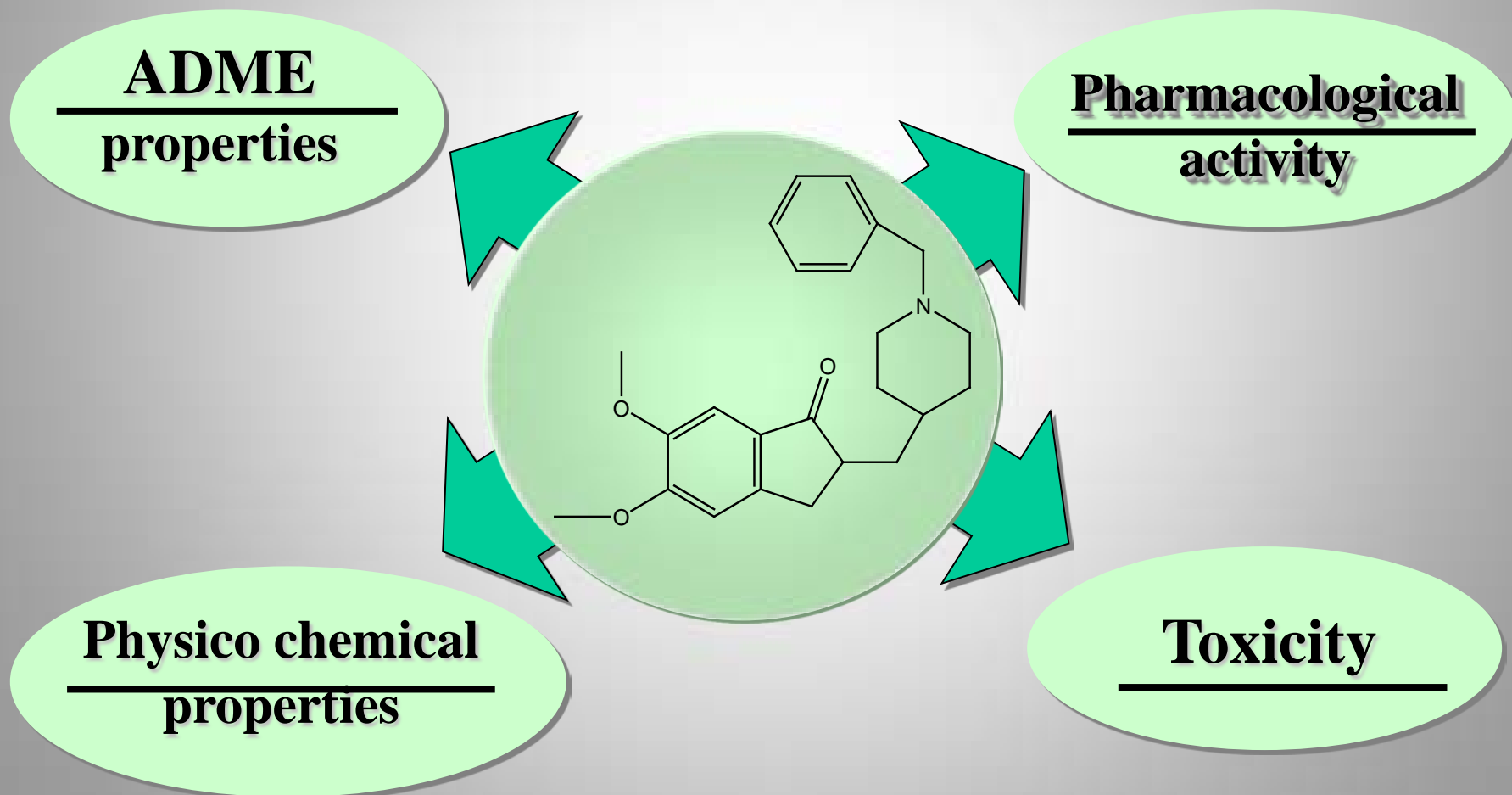
**High classification and prediction rate**

**by**

**KY-methods and Tailor made modeling**

# “Integrated” concept

## ■ Drug properties and compound structure

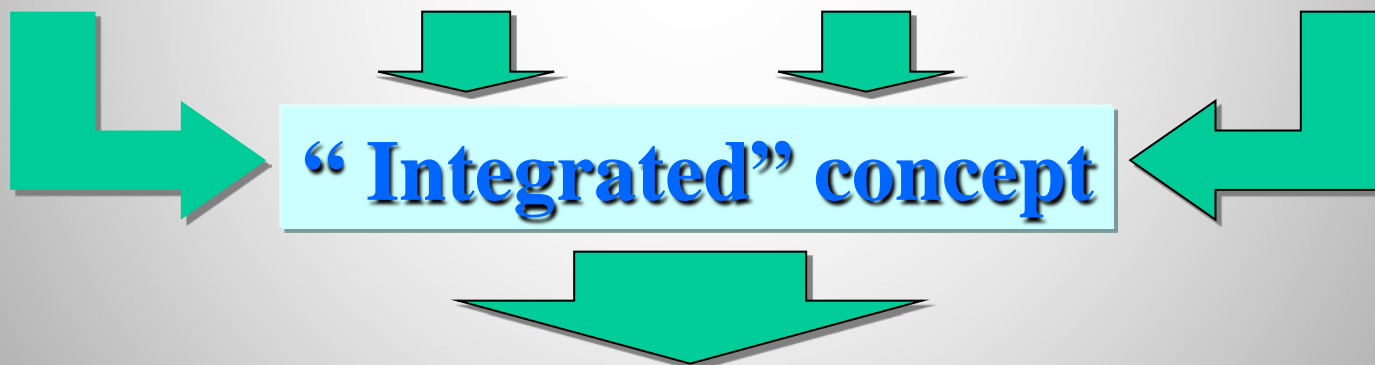


# “Integrated” concept

## ■ “Integrated” concept for drug development

Activity + ADME + Toxicity + Property

All drug properties shall be considered at the same time



“Integrated” in silico screening & drug design

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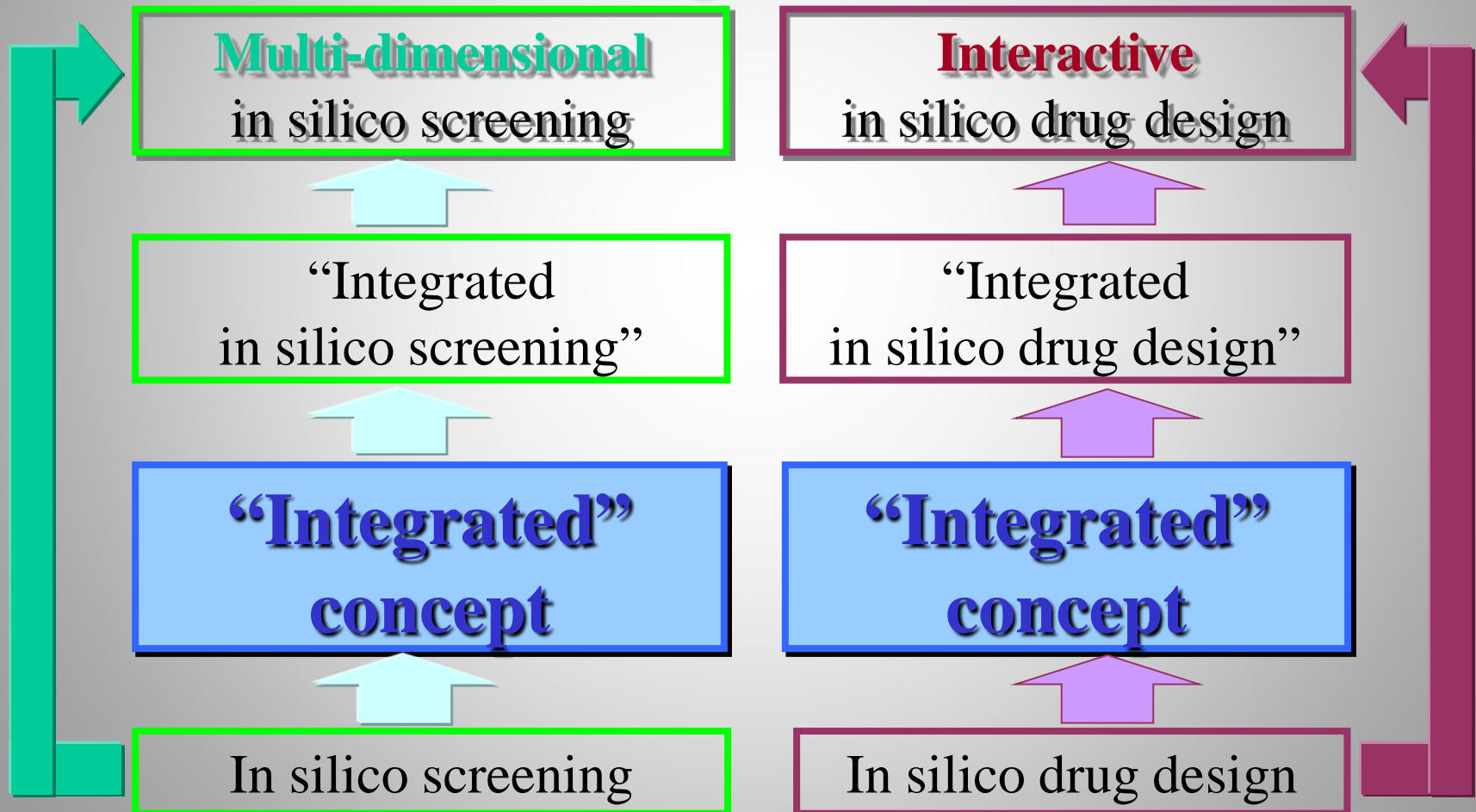
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*Application pattern of integrated concept*

## Two application style of “Integrated”



# Application pattern of integrated concept

## “Integrated” in silico screening

One-dimensional screening

one activity / compound

A	B	C	D
Order Col	Structure	R1 Label	Result (alpha 1)
1	<chem>c1ccc(cc1)C(=O)c2ccccc2</chem>	Phenylacetate	1671.08
2	<chem>c1ccc(cc1)C(=O)c2ccccc2</chem>	Phenylacetate	1722.88
3	<chem>c1ccc(cc1)C(=O)c2ccccc2</chem>	Benzoylvinyl	2536.82
4	<chem>c1ccc(cc1)C(=O)c2ccccc2</chem>	Phenylacetate	2555.84
5	<chem>c1ccc(cc1)C(=O)c2ccccc2</chem>	Phenylacetate	2576.31
6	<chem>c1ccc(cc1)C(=O)c2ccccc2</chem>	Phenylacetate	2576.31
7	<chem>c1ccc(cc1)C(=O)c2ccccc2</chem>	Phenylacetate	2586.71
8	<chem>c1ccc(cc1)C(=O)c2ccccc2</chem>	Benzamido	3739.95
9	<chem>c1ccc(cc1)C(=O)c2ccccc2</chem>	Carbamoyl	3775.32
10	<chem>c1ccc(cc1)C(=O)c2ccccc2</chem>	Bromo	3777.35
11	<chem>c1ccc(cc1)C(=O)c2ccccc2</chem>	Benzylidene	3782.45
12	<chem>c1ccc(cc1)C(=O)c2ccccc2</chem>	Benzo	3786.09
13	<chem>c1ccc(cc1)C(=O)c2ccccc2</chem>	Carbamoyl	3790.39
14	<chem>c1ccc(cc1)C(=O)c2ccccc2</chem>	Phenozymet	3790.74
15	<chem>c1ccc(cc1)C(=O)c2ccccc2</chem>	Carbamoyl	3805.29

**Conventional approach**

Multi-dimensional screening

multiple activities

" ADME

" toxicities

" properties

/ compound

A	B	C	D	E	F	G	H	I	J	K	L
Order Col	Structure	R1 Label	Result (alpha 1)	Result (alpha 1)	BOA	CYP1A9	CYP3A	Carcinogenicity	AMES	logP	logD
1	<chem>c1ccc(cc1)C(=O)c2ccccc2</chem>	Phenylacetate	1671.08	1839.2	1647.09	1	0	1	0	2.36012	-0.341246
2	<chem>c1ccc(cc1)C(=O)c2ccccc2</chem>	Phenylacetate	1722.88	1878.38	1864.05	1	0	1	0	2.82751	-0.321069
3	<chem>c1ccc(cc1)C(=O)c2ccccc2</chem>	Phenylacetate	2555.84	2768.54	2674.39	1	0	1	0	2.390	-1.42444
4	<chem>c1ccc(cc1)C(=O)c2ccccc2</chem>	Phenylacetate	2576.31	3073.91	2713.06	0	1	0	0	3.505	2.22775
5	<chem>c1ccc(cc1)C(=O)c2ccccc2</chem>	Phenylacetate	2576.31	3073.91	2713.06	0	1	0	0	2.523	2.19323
6	<chem>c1ccc(cc1)C(=O)c2ccccc2</chem>	Phenylacetate	2576.31	3073.91	2713.06	0	1	0	0	2.523	2.19323
7	<chem>c1ccc(cc1)C(=O)c2ccccc2</chem>	Phenylacetate	2586.71	3073.91	2713.06	0	1	0	0	2.555	1.61158
8	<chem>c1ccc(cc1)C(=O)c2ccccc2</chem>	Benzamido	3739.95	4080.55	3223.85	0	0	1	0	1.155	1.57861
9	<chem>c1ccc(cc1)C(=O)c2ccccc2</chem>	Carbamoyl	3741.14	4020.71	3760.16	0	0	0	0	-0.38846	2.00594
10	<chem>c1ccc(cc1)C(=O)c2ccccc2</chem>	Carbamoyl	3775.32	4369.63	3205.43	0	1	0	0	-1.19859	2.06413
11	<chem>c1ccc(cc1)C(=O)c2ccccc2</chem>	Bromo	3777.35	3789.94	4108.98	1	0	0	1	1.38841	-0.53316
12	<chem>c1ccc(cc1)C(=O)c2ccccc2</chem>	Benzylidene	3782.45	4182.23	4106.3	0	0	1	0	1.05442	0.364083
13	<chem>c1ccc(cc1)C(=O)c2ccccc2</chem>	Benzo	3786.09	4006.94	3935.08	1	0	0	1	2.11057	0.204521
14	<chem>c1ccc(cc1)C(=O)c2ccccc2</chem>	Carbamoyl	3790.39	4247.71	3922.87	1	0	0	0	-0.657456	0.093304
15	<chem>c1ccc(cc1)C(=O)c2ccccc2</chem>	Phenozymet	3790.74	4230.52	3270.94	0	1	0	0	2.46775	1.10953
16	<chem>c1ccc(cc1)C(=O)c2ccccc2</chem>	Carbamoyl	3805.29	4080.55	3223.85	0	0	1	0	-1.29534	2.49536

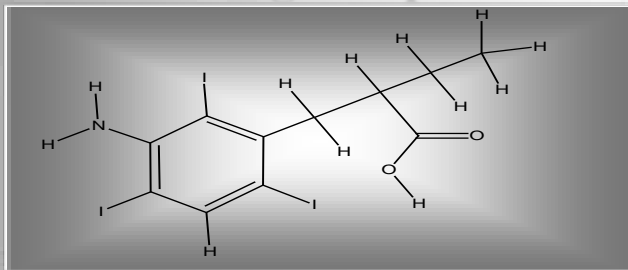
**Next-generation approach**

# Application pattern of integrated concept

## “Interactive and real-time” drug design

\* Check the effects of structure modifications on compound properties real-time

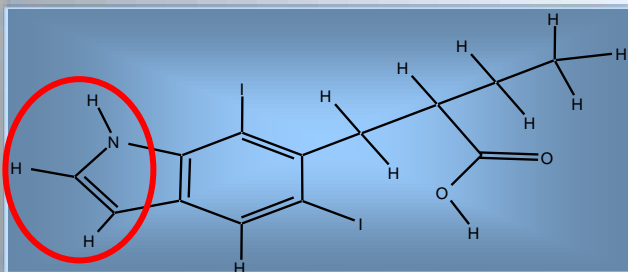
Starting compound



modification



activity  
ADME  
toxicity  
property



Modified compound

antibacterial	Anti-inflammatory	anticancer	. . . . .	pesticide
carcinogenicity	Ames test	LD50	. . . . .	others

ADME and properties

Caco-2	BBB	CYP
LogP	pKa	LogD <sub>7.4</sub>

antibacterial	Anti-inflammatory	anticancer	. . . . .	pesticide
carcinogenicity	Ames test	LD50	. . . . .	others

Information on different properties of different compounds is available anytime



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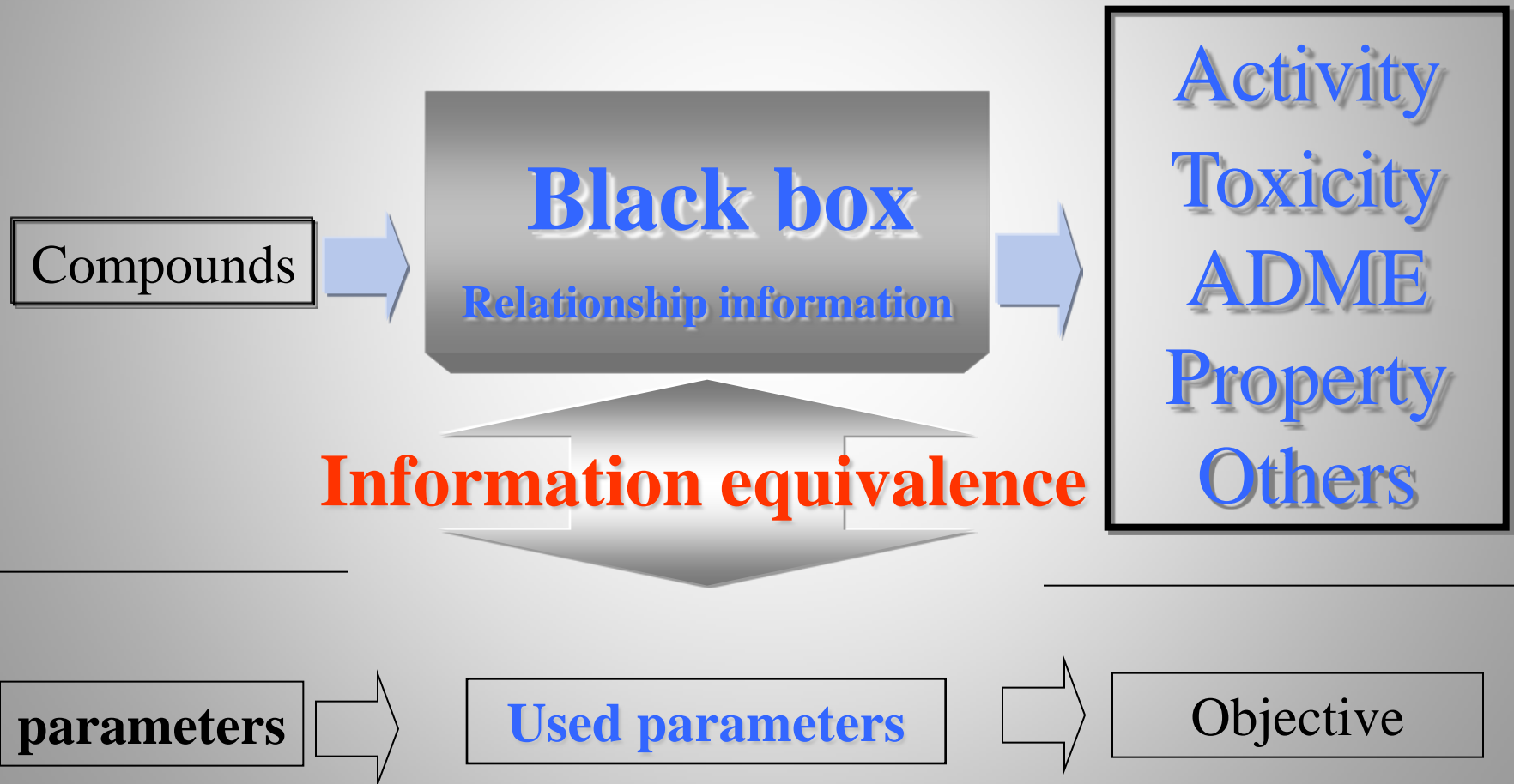
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## *Multivariate and pattern recognition*

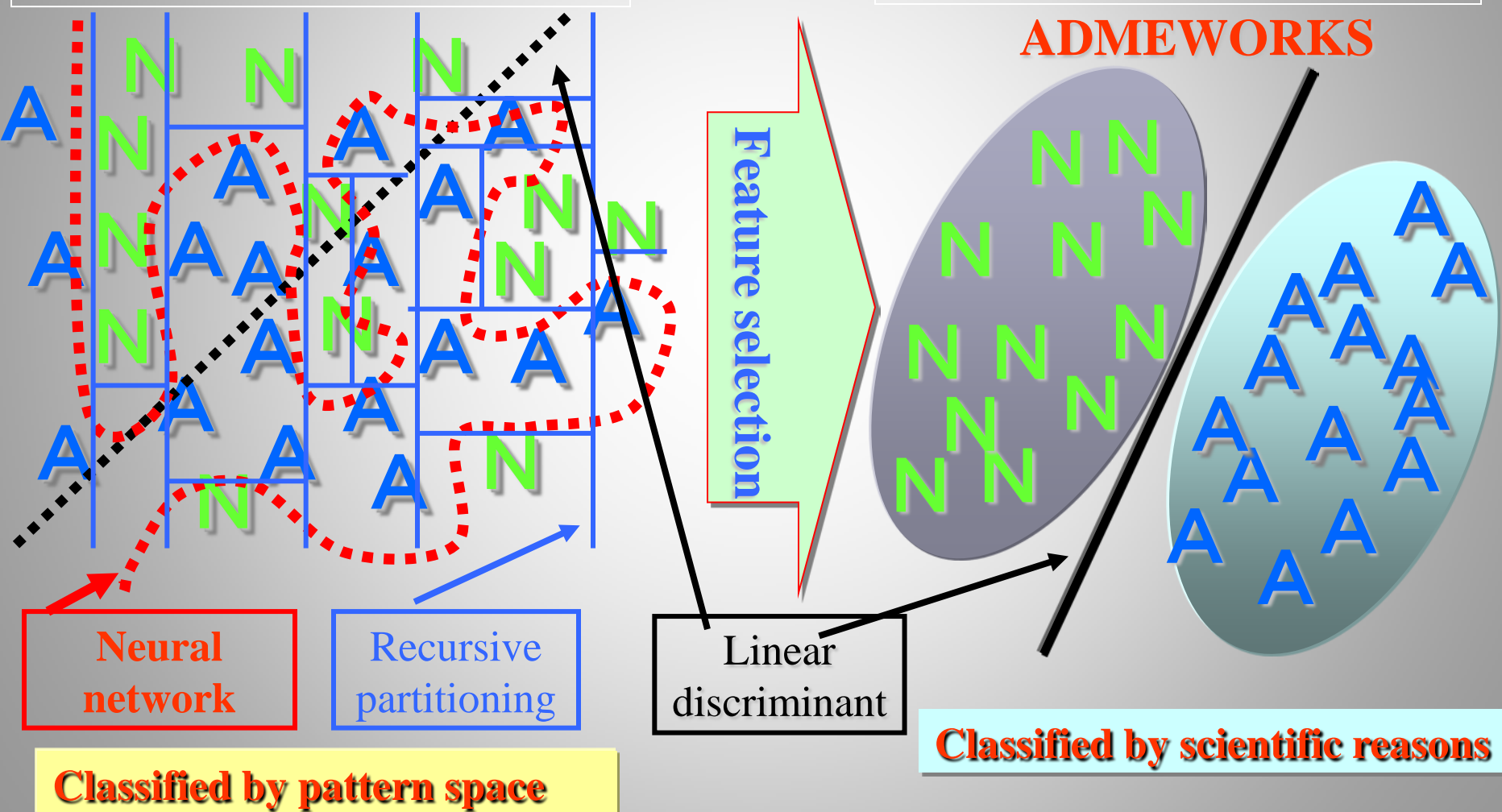
### ■ Basic principle of data analysis by MVA & PR



# Simple classification and scientific classification

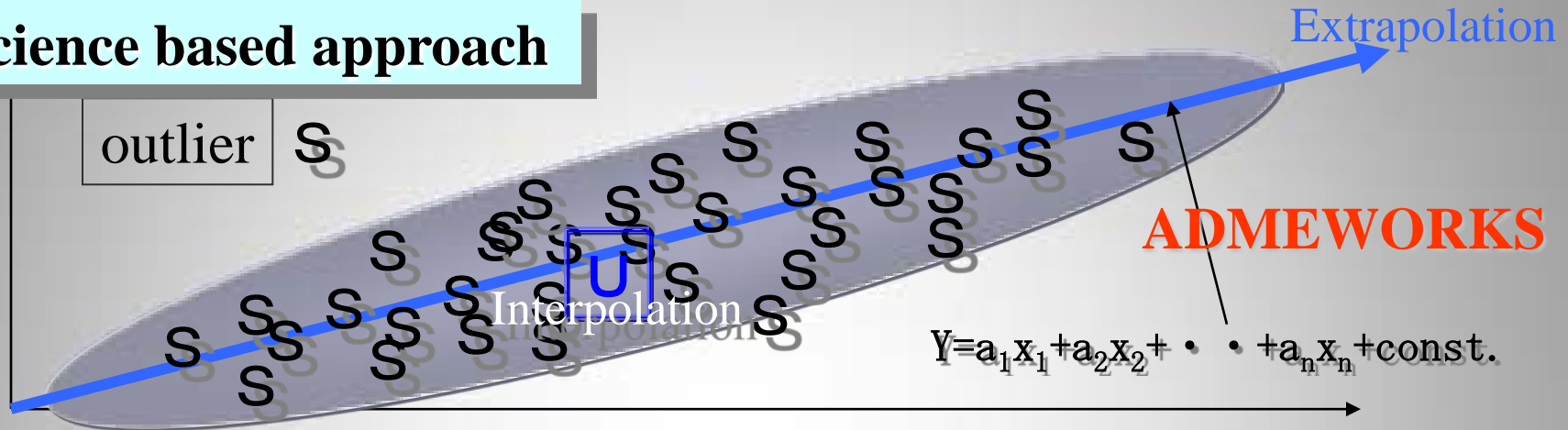
Pattern space impossible to be classified by linear discriminant

Pattern space classified by linear discriminant

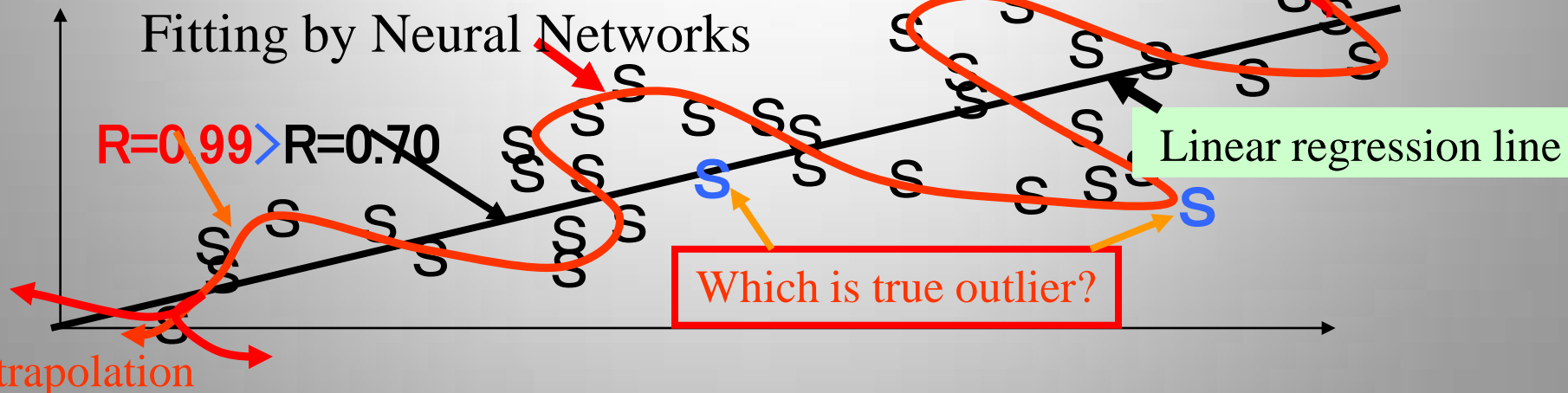


# Simple fitting and scientific fitting

## Science based approach



## No science based approach



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