



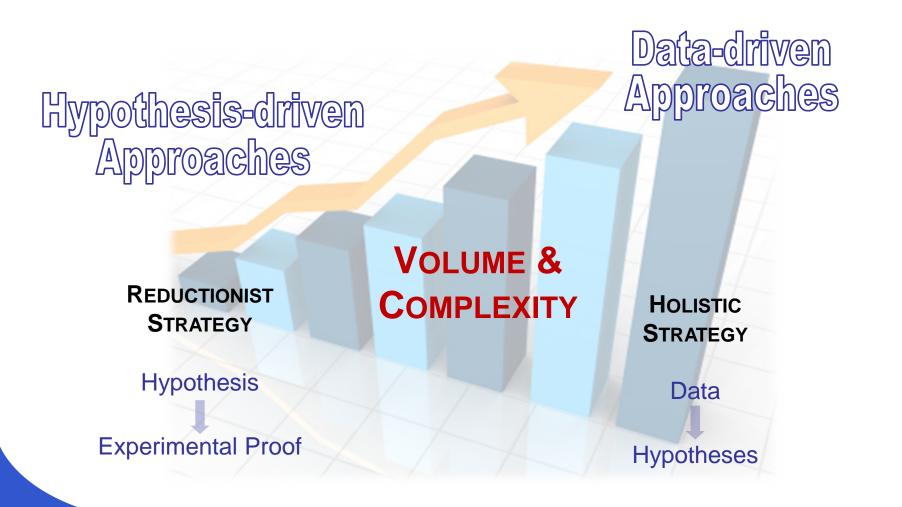


Swiss Institute of Bioinformatics

MULTIOMICS
DATA ANALYSIS
AND INTEGRATION

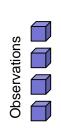
The Omics Data Explosion

Modern scientific technologies are able to generate massive datasets to describe specific phenotypes illustrating a biological phenomenon

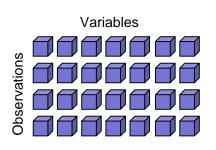


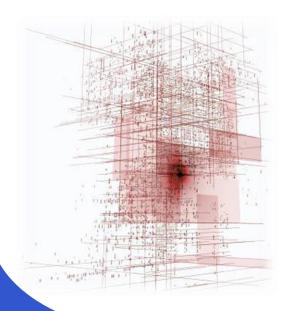
Data Structures

 One-way data is a vector, with a single data value for each element of the single dimension (n)



 Two-way data is a matrix, with a single data value for each element of two separate dimensions (n,p)





High dimensionality (n << p)
Multicollinearity between variables
Missing values
Biological/analytical variability

Adding extra dimensions leads to an exponential increase of the hypothesis space size → Relevant hypotheses become harder to find



1162_mg	,367.1585, mz,	367.1582, ma	367.1564, mz_3	67.1542 mg	369.1745, mz_	369.1742, ma_3	169.174_ma_	169.1768, mr_3	169.1752, mz_	369.1748, ma	369.1746; mz_	79.1243; mz,	381.1387, mc_38	1.1386; mr_381	.1371, mr_381.1	Slync	83.1535, mc	_363.1522, mc	c_383.1558; m	u_383.1539, m	z_383.1536, mo	c_195.1891, ma	411.1899.1	ur_411.2027	me_411.202_	ma_411.2017	mz_411.199_m	u_411.1975,	me_411.1963, me
1.0022	65.2462	3.1218	0	0	8.3391	11.1908	0	4.8271	0.0422 18.7759	216.2277	1.9264	0	2.1844	0 13	2788 2372	0 1	35.7473 06.5441	5.3544	3.4975	2.8636	194.463	0.0132	3.1101	0.2557	33.4228 18.3515	3.1082	16.9477	0.7498	0.5656
1.0008	305.512 53.0684	3.2197	0	0	0.9537 5.9542	329.8035 0	5.387 5.1783	7.8381 6.0957	7.0862	36.5744 22.0345	1.0868	0.8573	1.323		6718 0.0 9239	649 0 1	11.5528 90.4516	4.8486 3.9037	3.1155 8.8391	47.5709 5.5977	63.1034	3.7812 5.217	1.5514 3.0626	0	5.7215 35.0349	5.9424 22.473	7.7964 7.8913	1.8708	0
10061	93.7759	1.4907	0.0938	0	0	0	0	1.8158	1.8313 8.585	158.6447	7.6411	0	0 1761	-	8927 0.1 4683	808	38.5582	0.6565	0.4982	12.9724	20.5858 78.8553	0.8388	0	0.0886	18.5188 33.9754	7.1687 25.9764	2.3931	0.0815	0
0	70.7937	1.4564	0	0	0.0015	0	0	0	8.3656	38.3722	0	0	0	0 9	4768 2.8	787	94.3667	3.3108	3.6985	1.5106	107.5066	0	0	0.0811	11.3394	16.3762	3.1366		0
1.0058	22.6279		11.1753	0	6.9895 8.5762	0	0.4628	2.3772 6.5236	0 2354	59.7969 55.8998	0	0	0.5895	0 10	7631 2397	0	85.8655 482.573	3.631	4.2178 27.3977	3.1539	33.5813 164.5342	0.6343	1.4496	1.3654	13.2611	3.1441	9.1128		0
0	40.1099	262.0893	0	0.4015	0	38.409	12.6279	-	66.0515 31.1883	61.5895 93.2031	1.6042	0	1.3081	0 13	7394 0.3 7558		86.4922 42.6799	0 5.0787	0 3.415	4.9247	75.4759 69.3827	2.3389	8.2933	0.2757	13.8512	13.0941	3.8502	0.4437	0
0	13.8118	0	0.1747	0.0221	0	0.0209	0.0125	3.9359	3.6414	66.3458 74.0985	0	0.0481	1.3571		0504 3202 0.1	0	48.1999 78.1867	1.0612 2.7167	2.8438	2.2391	14.7141	0	5.2798	1.8122	86.6192	133.0639 9.5814	31.7199		0
0	152.2111	2.8539	5.1867	1.4023	0.9815	0	0	3.2378	28.6053	58.1164	2.9236	0	ě.	0 40	9834	0	139.689	534.4629	17.007	17.1283 8.1836	17.2495	0.2315	7.6922	0	4.5871	0.7265	4.1785	0.2987	0
1.0018	58.8086 20.4214	0.965	0	0	0	0	3.4352	2.4383	4.8479	24.1163 16.573	1.3402	0	3.4417		A243 0.1 2715	0 0	47.1448 71.3835	2.6572	3.2572 4.5284	3.2599	57.8503 88.6554	2.956	4.294	9.8386	6.6242 19.0725	9.441 16.4192	3.4043	2.4342	0
1.5465	2.9691	0.4911	2.7082	0	34.3736	2.5216	3.0579	0	1.6468	24.9303	23.917	0	0	0 24	8283 6947	0 1	96.0284	2.4026	4.0047	1.8879	91.6364	0	1.5009 2.8705	0	30.9374	32.5929	6.7135 8.6724	0.2093	0 8 5024
1.0009	63.9296	6.9673	0.9964	1.6755	0 :	164.9046	0		11.0634	54.0371	0.4144	ō	2.6177		9965		74.0564	9.6993	3.6723	4.1736	0.795	0	28.1721	2.0309	35.3824	14.4612	2.3897	3.4355	1.1476
0	22.8643	1.763	0	0		0.0307	0	2.5247	7.375	42.118	2.5578	0	1.5097		5607 4646 0.2	517	18.8949 2.9787	3.2595	2.6693 6.5467	2.8774	73.3785 58.6602	1.8614 5.8242	8.311 2.0287		17.6353 64.5705	41.2504	8.0371 22.1257	2.6218	1.0548
0	156.6525 120.6455	2.3978	0.2315	0.6146	0 :	0.0457 284.5795	2.3157	19.2256		200.4843 114.2344	0.0507	0	0.76		3.002 1168 0.0	0 197 2	1.5152	1.5152 2.8648	2.9633 8.2794	5.925 1.7866	0.0691	0	4.4422 21.9515	2.7465	64.4542 50.0973	69.166 21.6358	29.044 54.4375	0.7575	1.1159
0	150.9772	3.699	0	0	0	0.4449	1.7273	3.7089	17.9766	221.0883	0	0	1.1884		4646 8672 0.0	0	2.8931	2.0045	3.2111	1.813	110.1572	4.3765	1.8965	0.06	15.0284	26.334	6.6456	1.7915	0
0	51.8569	1.7263	2.8873	1.0758	0	0	1.1401	3.5446	3.7421	41.9624	0	0.1795	0.7912	0 18	0859	0	412.589	5.767	18.9437	3.361	21.452	0	3.03	0	6.5762	5.1054	3.878		0
1.0043	143.5543 189.9846	2.4554	0	0	2.4144	0	7.463 0.3427		23.8789 18.1243	127.5873 58.6299	0	0.7254			8063 2275	0 1	15.4752 68.0498	4.1041	2.5775 3.4205	6.2826	64.0505 65.4893	3.2512 0	0.7312	0	27.2568 53.3242	8.5887 47.6494	2.5438 14.6029	0.0678	0
1,0009	13.3243	0.6368 350.3376	0	0	0.0243	0	0		14.2568 133.6651	67.5103 327.5936	0.1481	1.1789	0.5523		2455 #347 0.	0 301 2	2.0438	3.3934	5.7101 3.9131	1.0043	9.9461	0.0208	11.7098	1.1849	53.3018 18.3537	45.7426 14.5767	13.979	0.1798	0
0	1.1448	88.8417	2.0347	0	0.0069	0	0		110.6768	96.0098	3.4751	0	0	0 14	3712	0	26.2236	203.1489	7.634	4.3227	1.8919	1.5091	0.009	0	8.7398	0	25.2617	0	0
0	32.1498	0	0	0.7329	0	0	0.9628	1.7443	43.793	53.6039	0	0	1.7141	0 16	0585	0	76.8972	1.2312	3.3062	3.3935	0	0	3.4619	3.1907	63.596	37.004	15.1209	0.8123	3.8831
0	3.648	°	2.4399	0.2645	28.0016	2.6017	0 14	0.87 8641	2.3655	1.3902	31.7511 4.9528	4.9554	2.0601	2.9132	.4289 0.3 0.3505	002	73.0654	2.4229 0.4032	3.3362	0.547 D	7.6954	0.28	10.8119 7 0.0	2.1301 0119	143.2486 0	66.4603 2.7898	51.6171	5.15	0
4587	0	0.777	0.8753 2 29 0	0.2953	2.449	7 1.45	545	0 0	1.1722	4.4858	0	2.2206	0.9624	0.3672	1.5803	2.1	873	0.5947	0.2771	0	2.2058	0.261	8	0	0	6.2509	0	0	0
7766	0	0.7878	2	0.38 344		0	0	ů	20 1	3.1697	D. W	5631		2.7	dib	4.8	192		41					D	0.1747	5.0872	0	0	1.1731
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0495	0.0222	1.1112	2.16	1.3271	2.77	2.09	253	.65	-4	8.299	2.2247	.425	22777	0.636	7	0.0	035	0.244			56	0.27		700	0				0
4351	0.0319	0.5653	3.5931	2.25/1	1.559	9 1.07	713	0	0	2.3211	1.6624	1.3301	4.11	1.3718	0	0.	387	0.0336	0	0	1.595	0.27	0	0	1.3778				0.9829
1.423	0	0.7136	2.1562	0.1939		0	0 1.7	7224 0	0.9511	1.4706 9.5731	4.8704	35.0698	2.6951	1 6167	0.3767		0	0 2212	0	1.7622	2.2046	0.176	0	0	0 0201		_		0.0499
0068	0.1911		2.2703			0	0	ö	0 :	14.6697	0	4.3879	2.6466	0.9975	1.2166		o	0.2313	0	0.6319	2.4144		0	0	0	406	0.2		0
0	0.7126	0.3741	1.07	0.9052	1.27	0.66	0 24	0	0 :	10.4639	1.2758	3.3341	1.1327	0	0	1.5	969	0.0	0		1.6072	0		0	0	1.1962 5.8942	0.0284		0
9599	0		2.2708 1.0 2.6 1 0.9	0.9921			0		0		1026	, i	1.1327		0				0						0	11.4665	0.854		0
0	0.0023	0	0.9	0.2615			0 2.2	10.	0	3.3	1998	0	1.78	74	0.2815	A.	0		8		3.1588	0		0	0.0027	4.4405 1.9262			0.098
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1997 3225	0	0	2.6052	1.0925	3.332	2	8 0 Z:	259	0	9.4364	3.3322	7.8168	2.1627	0	0		0	0	0		1,9226	0.	0	0	0	0.8727 2.9742		0	4.1663
8615	0.0312	1.2259	2.1233	1.2611	2.802	5 1.48	343 1.8	1663	0.486	12.742	0	0	1.8663	0.2129	0.3432	0.9	904	0	1.8154	0	0	0.220	0 0.2	2301	0	0		0.0837	0
3934	0.0603	0.6418	1.6101	0.0459		0	0 1.	0	0	4.237	4.698	1.9128	0.2328	0.7635	0.0666		0	1.1431	0.0145	1.9464	3.0019	0.398	0	0	0	5.533 15.6753	0.0304	2.1504	0.2857
4654	0	1.3153	1.4715	2 9701	0.020	9	0	0	0	1.4966	3.9003	4 3565	0	2.5516	0.3551	0.	321	0.8608	0	0.0158	5.8417	1.854	4 0.0	3842	0 1578	0 1.7625		0.0443	0.0286
0	0.0012	1.1404	1.7374	0.8184		0 0.90	334 1.1	1175 1	2819	5.5131	1.4262	0	3.0096	0.8503	0.8303		ő	0.775	0	0	:2629	0.422	0	o	0	4.5818		0.2059	0
1057 9198	0	1.2161	0.5121 1.8837	0.8145		0	-	2379 9066 0	0	9.3872	3.096	1.5356	1.3711	An An			0		0	The state of the s	138			4	0	13.043		0	0
6826	0	1.4921	2.6644	0.6172		0 2.78	336 0.8	1229	0	9.8029	0	0	2.970	0	0.8503	1	19	2.5	- 6	1.2744	0.014			0	0	5.9304		0	0
3,8725	0.1432	0	2.2729	0.3072	1.5822	4.0817	2.6039	6317	0 0.33	1.5623	0	2.8978	1.607	9	0	7 1	1	0.7	0		1.838.		9	9	10.1384	1.3026	0	0.2387	3,0339
3.1846	0.1358	0	0	1.6141	0	0	0	1.3182	2.33	0 11.15	22 1.73	3 3.15 28 4.95	09 2.725	1.8715	0		6	0	0		3.1503	0.397	0	-	5.5355	0	0.0457	0	1.5479 4.1483
1.4851	0.4587	0	0	0.8753	0.2645	2.4497	1.4545	1.8641	0.172	2 4.48	58	0 2.2		0.3672	1.5803	2.1	873 0	5.5947	0.2771	0	2.2058	0.2618	0	0	6.2509	0	0	0	0
3.4329 4.1611	2.7766	0	0.7878 2.4405	2.9857	0.3896 2.3445	0	0	. 0	0.127	0 10.60 1 3.16		0 43 8.56	0 0.48 35 2.510	9 2.6805	0.4878	0.9 4.8	192 697	0	0.451	0	0	0	0	0.1747	5.0872	0	0	1.1731	1.854 2.4527
3.0883	0	0.002	0	2.7909	0	2.7131	1.6764	1.0274		0 11.02		0 3.77	14 2.201	7 (0		0	0	0.5106	0	0 2369	0.0915	0	0.0761	1.3362	0	0	0.128	2.6288
6.1173	0	0	0.1349	1.9858	0.612	0	0	0	1.259	9 8.42	46 3.1	1 7.5		0.3312	0.1581		0	0	0	1.9589	0	0	0	0	20.1134	0	0	0	0
3.8518 3.9748	1.0495	0.0222	1.1112	2.1473 1.4982	1.3271 2.2571	2.7774	2.0953	0.4026	0.486	4 8.2 4 11.13	94 2.22	0 4.4 17	0 2.255	0.6363 5 1.9231	0	0.0	0	0.344	0	0	0.9289	0.272	0.1708	0	1.0959	0.2673	0	0.9829	2.1583 1.9853
3.313	0.4351	0	0.5653	3.5931 2.1562	0.1939	1.5599	1.0713	1,7224	0.951	0 2.32 1 1.47	11 1.66 06 4.87	24 1.33 34 35.04	01 4.1 98 2.695	1 1.3718	0	0.	387 0 0	0.0336	0	1.7622	1.595 2.2046	0	0	1.3778	3.3102	0.2058	0	0.0499	2.7365 2.9877
6.7725	1.5586	0 1011	1.3408	2.469	1.1069	0		0)	0 9.57	31 2.56	0 43	95	1.6167	0.3767		0 0	0.2313	0	0.8319	2.3071	0.1761	0	0.0701	15.1827	0.2009	0.0761	0	2.3545
3.6498	2.0008	0.7126	0.3741	1.0761	0.9052	1.2789			,	0 10.46		0 3.3	41 1.132	7 0.9975	1.2165	1.5		0.0768	o	0	1.6072	0	0	0	1.1962	0.0284	0	0	2.0364
2.6218 2.6088	0.687	0.0367	1.7743	2.6407 1.0388	0.9921	0	0			0 13.2 0 3.76			0 74 7.532	3 0	0	3.3 2.3		0	0	0.6419	2.2453 4.0366	0.0571	0.1444	0	5.8942 11.4665	0.8541	0	0	2.2396 2.6062
1.044 4.7031	0	0.0023	0	0.9775	0.2615	0				0 3.73 0 10.32						0.0	195	0	0	0	3.1588 4.0463	0.7984	0	0.0027	4.4405 1.9262	0	0.1638	0.098	1.1841 2.9208
0	0	0	0	0	0.3483	2.1087	0	0		0 6.2	37	0 2.15	91		0		0	4.62	1.0403	0	1.8426	0	0	0	3.5078	0	0	0	0
3.401 2.5763	0.1997	0	0	1.8668 2.6052	0.5574 1.0925	0.1763 3.3322				5 6.0 0 9.43						1.9	959	0	0	2.2874	1.9226	0.0846	0	0	0.8727 2.9742	0	0	4.1663 0	4.1663 2.0417
3.2126 4.3448	0.8615	0.0312		2.1233	1.2611 0.0459	2.8025	1.4843	1.8663	0.48		42	0	0 1.866 0 4.868	0.2129		0.9			1.8154 0.0145	0 1.9464	0 2.897	0.3985	0.2301	0	5.533	0	0.0837 2.1504	0.2857	2.4299 2.7065
3.0662	0.3934	0	0.6418	1.6101	0	0	0	0)	0 4.2	37 4.6	88 1.90	28 0.232	8 0.7635	0		0 1	.1431	0	0	3.0019	0	0	0	15.6753	0.0304	0	0	1.9883
2.2408 2.6233	0.4654	0	0	1.4715 1.7302	2.8701	0		0		0 1.49 0 9.72	67	0 4.35		1.3646	0.8503	0.	0	0 8038.0	0	0.0158	5.8417	1.854 0.4223	0.0842	0.1578	1.7625	0	0.0443	0.0286	1.4393
	0	0.0012	1.1404	1.7374 0.5121	0.8184						31 1.42 0 3.0		0 3.009 0 1.371				0	0.775	0	6.6701	2.2629 4.638	0.352	0	0	4.5818 0	0.1568	0.2059	0	2.0841
3.3068 1.317	0.1057	0																	-										
3.3068 1.317 3.8275 5.7344	0.1057 1.9198 1.6826	0	1.2161	1.8837 2.6644	0.8145 0.6172	0		1.9066		6 9.38 0 9.80		0 1.5	56 2.423 0 2.970			2.0	0 249 2	0	0	1.2744	2.0147	0.3476	0	0	13.043 5.9304	0.6897	0	0	2.2921 2.4842

Knowledge Discovery In Omics

Analytics



Data Production

- ✓ Sample preparation
- ✓ Data acquisition

Data Processing

- √ Signal extraction
- ✓ Filtering
- ✓ Normalisation
- ✓ Annotation

Information Content Signal





Knowledge

Biological Interpretation

- ✓ Extract relevant information
 - ✓ Link to existing knowledge
 - ✓ Biological validation

Chemometrics



Multivariate Analysis

- ✓ Exploration
- √ Classification
- ✓ Pattern Recognition
- √ Variables contribution

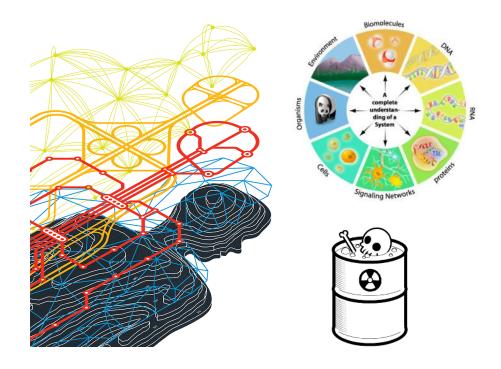
Bioinformatics

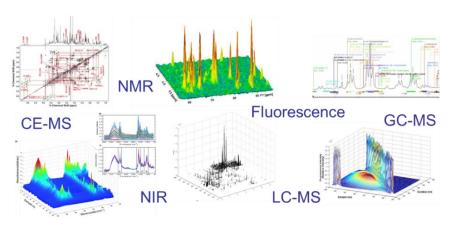
Multiple Data Sources Omics

- ✓ Different biological scales
 - ✓ Cell/tissue/organism
 - ✓ Systems biology

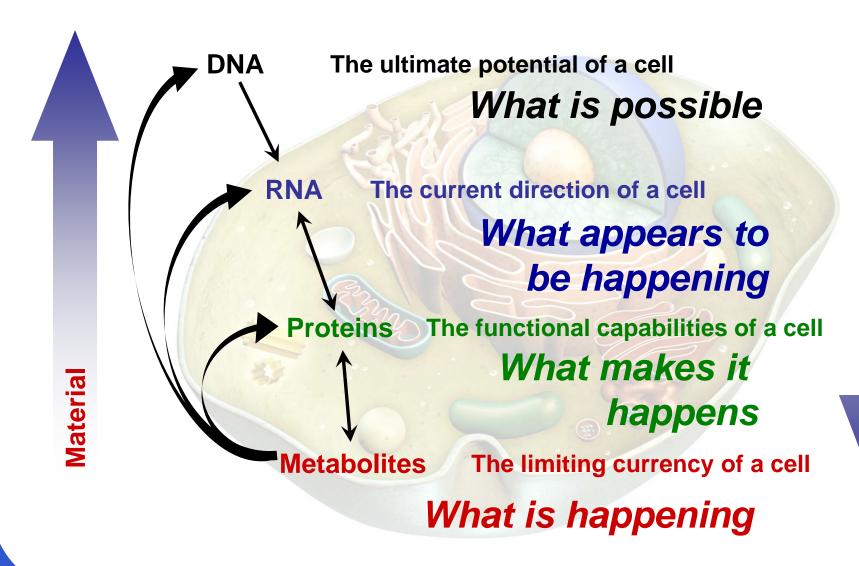
- ✓ Different stages of a process
 - ✓ Dose
 - ✓ Toxicity
 - ✓ Disease progression

- ✓ Different analytical techniques
 - ✓ Heterogeneous data
 - ✓ Separation or spectral methods





MultiOmics & Systems Roles



Information

Embracing Complexity

How does a complex system work?



Examine separately springs, gears, shafts, etc. how they fit together

or





Consider all the elements at once and how they fit and interact together

DATA INTEGRATION

MULTIGROUP ANALYSIS

DATA FUSION

MULTITABLE ANALYSIS



MULTIVIEW ANALYSIS

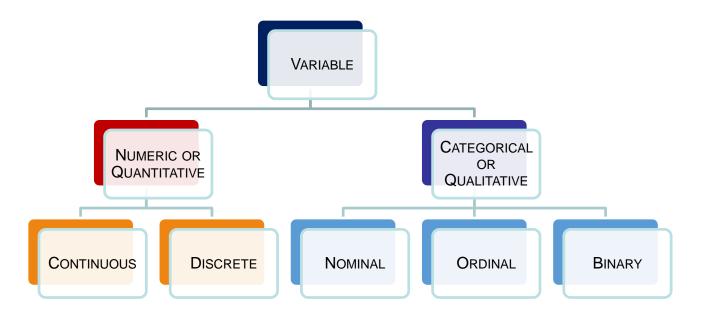
MULTISET ANALYSIS

MULTIBLOCK ANALYSIS





Nature Of The Data



QUANTITATIVE

- Continuous: numeric variables that can take any value between a certain set of real numbers
- Discrete: numeric variables that only consist of integers

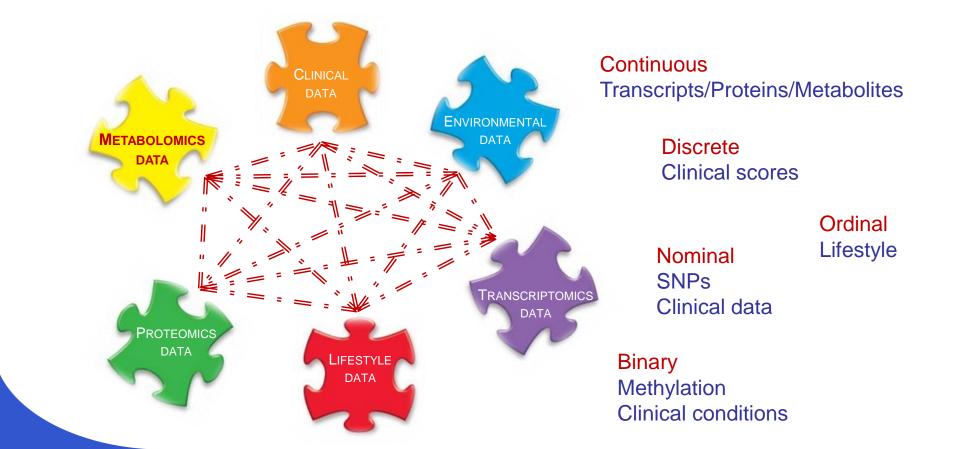
QUALITATIVE

- Nominal: categorical variable that cannot be ranked
 - Ordinal: categorical variable that can be ranked
- Binary: categorical variable that is either true or false

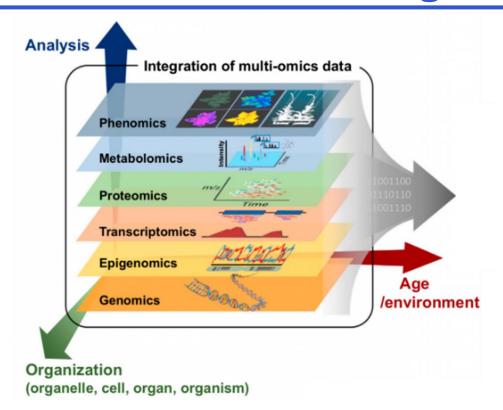
Data Homo/Heterogeneity

Homogeneous data: data blocks all measured on the same scale e.g. quantitative data

Heterogeneous data: data blocks measured on different scales e.g. quantitative, ordinal, qualitative, binary



MultiOmics Data Integration

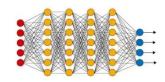


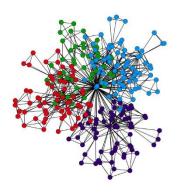
AIMS

- Molecular signatures
- Biological processes
- Mechanistic insights
- Interplay between layers
 - Holistic view

METHODS

- Matrix factorization
- Network-based approaches (multiplex, multilayer)
- Bayesian approaches
- Machine learning (embeddings)



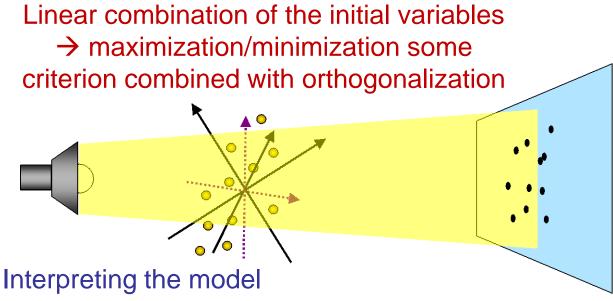


Methods Based On Components

Data High Dimensionality
Variables Correlations
Biological Variability
Experimental Noise

Projection methods

- ✓ analyze datasets of high dimensionality
- ✓ provide knowledge about systems
- ✓ find unsuspected relationships
- summarize the data with a small number of factors



- Visualize the samples' distribution
- Visualize correlations between variables

Model Objectives

Search for a subspace providing an effective representation of the data Build a multivariate model (PCA, PLS, OPLS)

Analyse the model



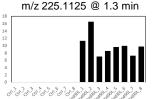
Search for patterns/groupings Prediction performance

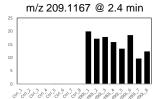
Evaluate the variables' contributions

Rank the variables



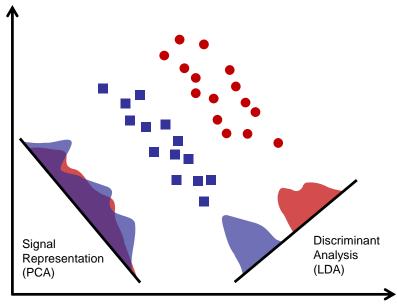
Find the most relevant biomarkers



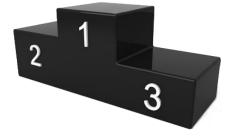


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Dimension 2



Dimension 1



→ MOLECULAR SIGNATURES