Metabolomics/Metabonomics Literature Roundup 2005

Tobias Kind
fiehnlab.ucdavis.edu

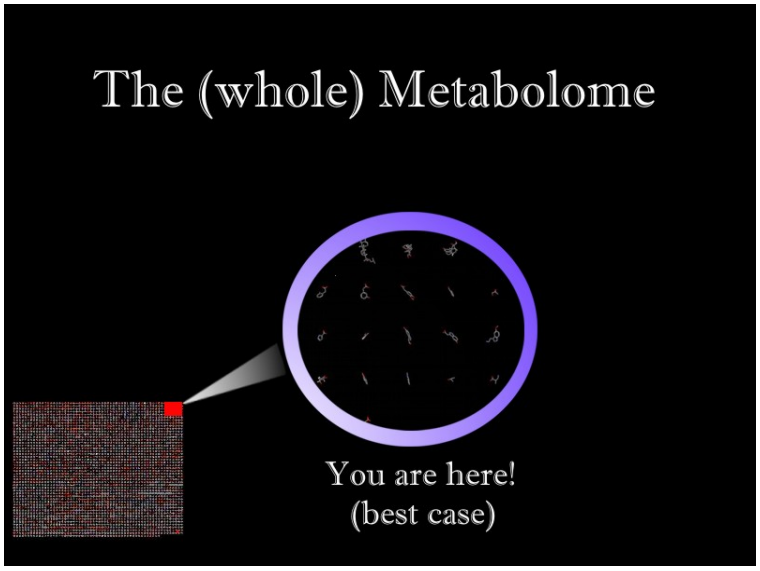
Index

Report December 2005, 14 pages

Introduction

Metabolomics and Metabonomics try to analyze metabolic responses in all life forms in a comprehensive manner (www.metabolomicssociety.org). Metabolites are the intermediates and products of metabolism (http://en.wikipedia.org/wiki/Metabolite) and usually defined as small molecules with a molecular mass up to 2000 Dalton. Qualitative, quantitative and time course experiments are done with the help of complex analytical techniques like NMR, GC-MS, LC-MS or FT-IR. Metabolomics is part of the life science tree: Genomics (gene level), Transcriptomics (mRNA level) and Proteomics (protein level). Bioinformatics and Chemoinformatics help to solve the complex mathematical and statistical problems of Metabolomics. Both terms (Metabonomics and Metabolomics) are defined in a different way by different groups which led to a fancy "war of the words". The author personally beliefs that both terms have the same intention: "Solving the metabolome".

This report gives an in-depth analysis of the literature in the field of Metabolomics/Metabonomics from **first citations up to the year 2005**. The field of "metabolomics" itself is probably older than 3000 years[1]. The renaissance started with modern analytical techniques in the 70s of the last century. Both terms were used more frequently during the year 2000.



[1] *Clinical features similar to diabetes mellitus were described 3000 years ago by the ancient Egyptians. The term "diabetes" was first coined by Araetus of Cappodocia (81-133AD). Later, the word mellitus (honey sweet) was added by Thomas Willis (Britain) in 1675 after rediscovering the sweetness of urine and blood of patients (first noticed by the ancient Indians).* History of diabetes mellitus. Ahmed AM, Saudi Med J. 2002 Apr;23(4):373-8.

1) General Numbers

The following portals were used for analysis:

Web of Science (WOS) (http://portal.isiknowledge.com/)

Google Scholar (Google) (http://scholar.google.com/)

CAS Scifinder (CAS) (https://scifinder.cas.org/)

The results here usually refer to the number of publications. Due to duplications or reference problems in the databases certain results may overlap. Author names or institute names were sometimes misspelled. In these cases results were adjusted to the best knowledge, without bias.

Web Of Science
Metabonomics: 234 records. TS=(metabonomics)
Metabolomics: 376 records. TS=(metabolomics)

Google Scholar
Results: 670 for metabonomics.
Results: 1700 for metabolomics
Results: 189 for metabonomics AND metabolomics

CAS Scifinder
Metabonomics and Metabolomics: 1454 results
Single authors involved: 2604
Single molecules involved: ~1000 (~9000 sequences excl.) (compared to KEGG ~20.000)

Metabonomics: 307 records (citing 4766 other publications and cited by 799 other publications)
(281 different molecules/sequences involved in research)

Metabolomics: 568 records (citing >10000 other publications and cited by >1200 publications)
(831 different molecules/sequences involved in research)

2) Country Analysis

According to Web of Science the leading (publishing) countries in the field of **metabolomics and metabonomics** are:

Country	Publications	Percentage
USA	225	39.80%
England	170	30.10%
Germany	58	10.30%
Netherlands	41	7.30%
Japan	38	6.70%
Canada	26	4.60%
Switzerland	24	4.20%
Denmark	19	3.40%

According to Web of Science the leading (publishing) countries in the field of **metabonomics:**

Country	Publications	Percentage
England	113	48.30%
USA	102	43.60%
Germany	9	3.80%
Switzerland	9	3.80%
Netherlands	8	3.40%
Sweden	8	3.40%
China (PR)	7	3.00%
France	6	2.60%

According to Web of Science the leading (publishing) countries in the field of **metabolomics**

Country	Publications	Percentage
USA	144	38.30%
England	76	20.20%
Germany	52	13.80%
Japan	36	9.60%
Netherlands	36	9.60%
Canada	22	5.90%
Switzerland	18	4.80%
Denmark	15	4.00%

3) Institute Analysis

According to CAS the leading institutions in the field of **metabolomics/metabonomics** are: the Imperial College, the Max Planck Institute in Golm and UC Davis. UC Davis is the leading campus among the University of California.

Name	Publications
Imperial College (UK)	129
Max Planck Institute of Molecular Plant Physiology (Germany)	51
UC Davis (US)	20

According to WOS the leading institutions in the field of **metabolomics/metabonomics** are:

Name	Publications
Univ London Imperial Coll Sci Technol & Med	76
Univ Calif Davis	26
Max Planck Inst Mol Plant Physiol	26
AstraZeneca	23
TNO	20
Univ Cambridge	17
Nestle Res Ctr	15
Chiba Univ	14
Univ Manchester	13
Waters Corp	12
Univ Oxford	11
Univ Wageningen & Res Ctr	10
Tech Univ Denmark	9
Univ Wales	9
Glaxo	9

According to Web of Science the 3 leading institutions (**metabonomics**) are the Imperial College, Astra Zeneca (drug company) and Waters (analytical devices).

Name	Publications
Imperial College (UK)	72
Astra Zeneca	23
Waters Corp	12

According to Web of Science the 3 leading institutions (**metabolomics**) are the Max Planck Institute for Molecular Plant Physiology in Golm, the UC Davis, the Chiba University (Japan) and the University of Cambridge.

Name	Publications
Max Planck (MPIMP) Golm (Germany)	26
UC Davis (USA)	24
Chiba University (Japan)	14
Univ Cambridge (UK)	14

4) Journal Fields

According to Web of Science most of the **metabonomics** studies were published in

Journal Field	Publications	Percentage
Chemistry, Analytical	55	23.50%
Pharmacology & Pharmacy	55	23.50%
Toxicology	46	19.70%
Biochemistry & Molecular Biology	38	16.20%
Biochemical Research Methods	27	11.50%
Biotechnology & Applied Microbiology	20	8.50%
Chemistry, Multidisciplinary	19	8.10%
Biophysics	17	7.30%
Cell Biology	14	6.00%
Spectroscopy	13	5.60%
Chemistry, Medicinal	8	3.40%
Nutrition & Dietetics	7	3.00%

According to Web of Science most of the **metabolomics** studies were published in:

Journal Field	Publications	Percentage
Biochemistry & Molecular Biology	74	19.70%
Biotechnology & Applied Microbiology	64	17.00%
Plant Sciences	59	15.70%
Biochemical Research Methods	40	10.60%
Chemistry, Analytical	40	10.60%
Cell Biology	29	7.70%
Nutrition & Dietetics	24	6.40%
Pharmacology & Pharmacy	24	6.40%
Genetics & Heredity	23	6.10%
Toxicology	19	5.10%
Food Science & Technology	18	4.80%
Biophysics	16	4.30%
Computer Science, Interdisciplinary Applications	11	2.90%
Mathematics, Interdisciplinary Applications	11	2.90%
Multidisciplinary Sciences	11	2.90%

5) Fields of Interest

According to CAS the following fields of interest were covered by **metabonomics and metabolomics**:

Field of Interest	Count
Metabolism	431
References not containing information for this analysis	266
Methods	250
Research Support, Non-U.S. Gov't	233
Animals	202
Genetics	188
Humans	181
Human	139
Genomics	120
Chemistry	117
Magnetic Resonance Spectroscopy	110
NMR spectroscopy	109
Proteomics	96
Proteins	95
Urine	94
Proteome	93
Physiology	91
Genome	88
Mass spectrometry	83
Principal component analysis	83
Metabolism, animal	77
Analysis	76
Research Support, U.S. Gov't, P.H.S.	75
Bioinformatics	74
Male	74
Rats	73
Liver	67
Urine analysis	65
Simulation and Modeling	62
*Genomics	59
Diagnosis	59
Gene Expression Profiling	57
Biomarkers	56
Spectrum Analysis, Mass	54
Toxicity	54
Magnetic Resonance Spectroscopy: MT, methods	53
Metabolism, plant	52
Models, Biological	52
*Metabolism	51
Saccharomyces cerevisiae	51
*Magnetic Resonance Spectroscopy	50

6) Top Terms for 2005

The associated terms for 2005 according to CAS are:

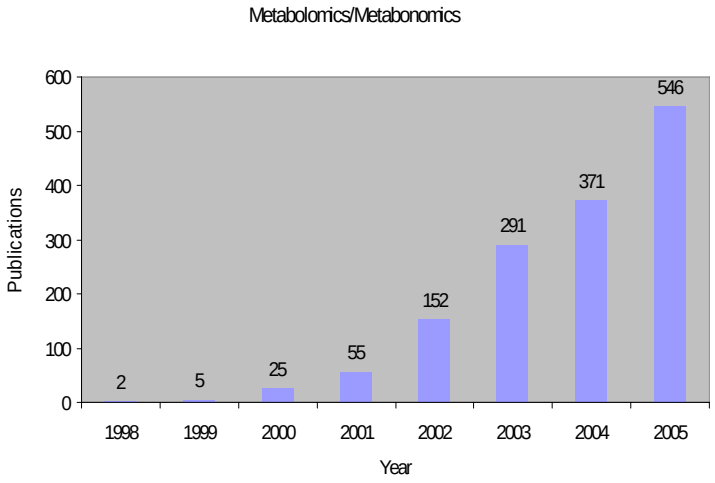
Metabonomics 2005 (108 publications)	**Metabolomics 2005 (248 publications)**
Animals	Metabolism
NMR spectroscopy	Genomics
Metabolism	Research Support, Non-U.S. Gov't
Urine	Proteomics
Principal component analysis	Genetics
Urine analysis	Humans
Humans	Animals
Metabolism, animal	Gene Expression Profiling
Proteomics	Bioinformatics

Top terms for metabolomics and metabonomics in general are:

Metabolomics	**#**	**Metabonomics**	**#**
metabolomics	257	Animals	68
review	147	Metabolism	68
analysis	74	methods	64
Genomics	60	NMR spectroscopy	58
Plant	56	Humans	56
Data	53	Urine	41
using	52	Magnetic Resonance Spectroscopy	40
spectrometry	51	Principal component analysis	40
Mass	48	Human	37
Metabolomic	47	Urine analysis	35
metabolic	46	Toxicology	31
metab	44	Rats	30
proteomics	43	Chemistry	28
metabolite	41	Liver	28
NMR	41	Toxicity	28
metabolome	39	Diagnosis	27
Systems	35	Research Support, Non-U.S. Gov't	27
gene	34	Genomics	25
Nutrition	33	Male	23
profiling	33	Metabolism, animal	23
Functional	31	Proteomics	23
biology	29	Genetics	21
metabolism	25	Drug toxicity	20
Human	24	Magnetic Resonance Spectroscopy: MT,	19
drug	23	*Magnetic Resonance Spectroscopy	18
expression	22	Biomarkers	18
metabolites	22	NMR (nuclear magnetic resonance)	18
New	22	Drug design	17
spectroscopy	22	drug effects	17
bioinformatics	21	*Magnetic Resonance Spectroscopy: MT,	16

7) Publications per Year

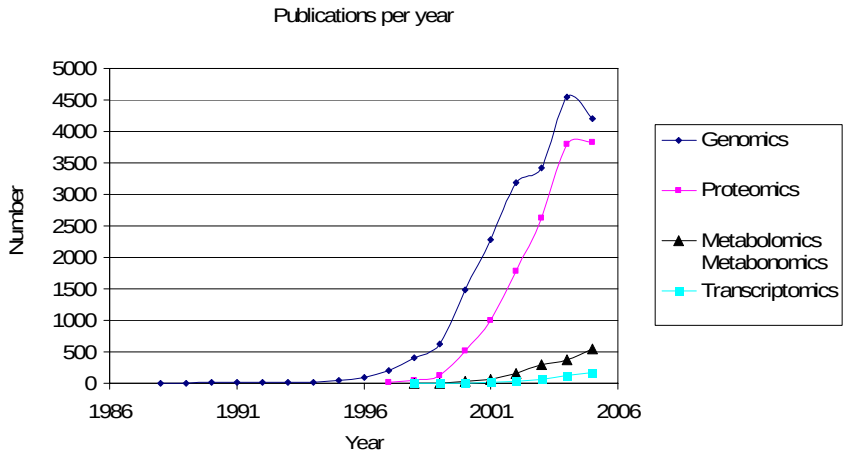
Number of publications per year in the field of **metabonomics and metabolomics**, according to CAS. Using a conservative factor of 1.5 the number of publications can jump up to 1000 in the year 2007. The number is very small compared to proteomics or genomics.



According to Web of Science and CAS the following publications were written:

Year	Metabonomics (WoS)	Metabolomics (WoS)	Metabonomics (CAS)	Metabolomics (CAS)
2005	79	162	108	248
2004	71	112	86	156
2003	47	63	55	95
2002	21	28	37	52
2001	9	10	8	13
2000	6	1	8	2
1999	1	0	2	0

Metabolomics is a true emerging field. Where genomics and proteomics almost reached a plateau in number of publications, metabolomics is still on its way (CAS data).



8) Journals

According to Web of Science (404 publications total) most articles for the fields of **metabonomics and metabolomics** were published in the following journals. According to CAS also 14 patents were filed. Compared to 6937 US patents for genomics and 546 US patents for proteomics this is a very small number.

Publication in Journal	Count
ANALYTICAL CHEMISTRY	20
JOURNAL OF NUTRITION	19
PHYTOCHEMISTRY	13
ABSTRACTS OF PAPERS OF THE AMERICAN CHEMICAL SOCIETY	11
ANALYTICAL BIOCHEMISTRY	11
BIOINFORMATICS	10
JOURNAL OF PHARMACEUTICAL AND BIOMEDICAL ANALYSIS	10
PLANT AND CELL PHYSIOLOGY	10
ANALYTICA CHIMICA ACTA	9
FEBS LETTERS	9
JOURNAL OF EXPERIMENTAL BOTANY	9
ANALYST	7
BIOMARKERS	7
CHEMICAL RESEARCH IN TOXICOLOGY	7
CURRENT OPINION IN CHEMICAL BIOLOGY	7
DRUG METABOLISM REVIEWS	7
JOURNAL OF PROTEOME RESEARCH	7
PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA	7
TOXICOLOGY	7
TRENDS IN BIOTECHNOLOGY	7
JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY	6
JOURNAL OF CHROMATOGRAPHY B-ANALYTICAL TECHNOLOGIES IN THE BIOMEDICAL AND LIFE SCIENCES	6
PLANT PHYSIOLOGY	6

9) Single Author Analysis

According to CAS the most publications in the field of **metabolomics** (out of more than 1000 different authors) were written by:

Author	Publications
German J Bruce	24
Saito Kazuki	23
Fiehn Oliver	22
Watkins Steven M	17
Mendes Pedro	17
Van Ommen Ben	15
Sumner Lloyd W	15
Kell Douglas B	15
Van Der Greef Jan	13
Goodacre Royston	12
Kopka Joachim	10

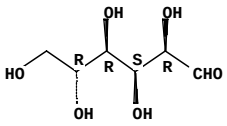
According to CAS the most publications in the field of **metabonomics** (out of more than 570 different authors) were written by:

Author	Publications
Nicholson Jeremy K	74
Holmes Elaine	64
Lindon John C	57
Robertson Donald G	26
Wilson Ian D	25
Antti Henrik	23
Bollard Mary E	20
Keun Hector C	17
Beckonert Olaf	13
Reily Michael D	13

10) Most Analyzed Molecules - Top 10

According to CAS the top 10 of the most cited compounds (out of ~1000) for the field of **metabolomics and metabonomics** are listed in the table. Interesting to know is that the KEGG database, which is an acknowledged database for metabolomics, contains more than 16000 molecules. That means the "metabolic sciences" itself were alive long before the "omics" era started.

Name	References
D-Glucose	78
Citric acid	52
Succinic acid	45
Lactic acid	43
L-Alanine	35
Glutamic acid	35
Taurine	35
Trimethylamine, N-oxide	34
L-Valine	33



Glucose is one of the most analyzed molecules in the world (not only in metabolomics). This is why certain journals do not accept any "new" technology for glucose analysis.

In **metabonomics** research 281 different molecules/sequences were involved in research, according to CAS.

In **metabolomics** research more than 831 different molecules/sequences were involved in research, according to CAS (9000 additional sequences were excluded).

11) Most Cited Publications for Metabonomics

According to Web of Science the most cited papers for metabonomics are:

1. Nicholson JK, Lindon JC, Holmes E
'**Metabonomics**': understanding the metabolic responses of living systems to pathophysiological stimuli via multivariate statistical analysis of biological NMR spectroscopic data
XENOBIOTICA 29 (11): 1181-1189 NOV 1999
Times Cited: 192
UC-eLinks

2. Nicholson JK, Connelly J, Lindon JC, et al.
Metabonomics: a platform for studying drug toxicity and gene function
NATURE REVIEWS DRUG DISCOVERY 1 (2): 153-161 FEB 2002
Times Cited: 172
UC-eLinks

3. Brindle JT, Antti H, Holmes E, et al.
Rapid and noninvasive diagnosis of the presence and severity of coronary heart disease using H-1-NMR-based **metabonomics**
NATURE MEDICINE 8 (12): 1439-1444 DEC 2002
Times Cited: 89
UC-eLinks

4. Gavaghan CL, Holmes E, Lenz E, et al.
An NMR-based metabonomic approach to investigate the biochemical consequences of genetic strain differences: application to the C57BL10J and Alpk : ApfCD mouse
FEBS LETTERS 484 (3): 169-174 NOV 10 2000
Times Cited: 74
UC-eLinks

5. Lindon JC, Nicholson JK, Holmes E, et al.
Metabonomics: Metabolic processes studied by NMR spectroscopy of biofluids
CONCEPTS IN MAGNETIC RESONANCE 12 (5): 289-320 2000
Times Cited: 65
UC-eLinks

6. Holmes E, Nicholls AW, Lindon JC, et al.
Chemometric models for toxicity classification based on NMR spectra of biofluids
CHEMICAL RESEARCH IN TOXICOLOGY 13 (6): 471-478 JUN 2000
Times Cited: 56
UC-eLinks

7. Nicholson JK, Wilson ID
Understanding 'global' systems biology: **Metabonomics** and the continuum of metabolism
NATURE REVIEWS DRUG DISCOVERY 2 (8): 668-676 AUG 2003
Times Cited: 52
UC-eLinks

8. Lindon JC, Nicholson JK, Holmes E, et al.
Contemporary issues in toxicology - The role of **metabonomics** in toxicology and its evaluation by the COMET project
TOXICOLOGY AND APPLIED PHARMACOLOGY 187 (3): 137-146 MAR 15 2003
Times Cited: 50
UC-eLinks

9. Aardema MJ, MacGregor JT
Toxicology and genetic toxicology in the new era of "toxicogenomics": impact of "-omics" technologies
MUTATION RESEARCH-FUNDAMENTAL AND MOLECULAR MECHANISMS OF MUTAGENESIS 499 (1): 13-25 JAN 29 2002
Times Cited: 49
UC-eLinks

10. Robertson DG, Reily MD, Sigler RE, et al.
Metabonomics: Evaluation of nuclear magnetic resonance (NMR) and pattern recognition technology for rapid in vivo screening of liver and kidney toxicants
TOXICOLOGICAL SCIENCES 57 (2): 326-337 OCT 2000
Times Cited: 46
UC-eLinks

12) Most Cited Publications for Metabolomics

According to Web of Science the most cited papers for metabolomics are:

1. Fiehn O, Kopka J, Dormann P, et al.
Metabolite profiling for plant functional genomics
NATURE BIOTECHNOLOGY 18 (11): 1157-1161 NOV 2000
Times Cited: 245
UC-eLinks

2. Raamsdonk LM, Teusink B, Broadhurst D, et al.
A functional genomics strategy that uses metabolome data to reveal the phenotype of silent mutations
NATURE BIOTECHNOLOGY 19 (1): 45-50 JAN 2001
Times Cited: 202
UC-eLinks

3. Fiehn O
Metabolomics - the link between genotypes and phenotypes
PLANT MOLECULAR BIOLOGY 48 (1-2): 155-171 JAN 2002
Times Cited: 170
UC-eLinks

4. Sumner LW, Mendes P, Dixon RA
Plant **metabolomics**: large-scale phytochemistry in the functional genomics era
PHYTOCHEMISTRY 62 (6): 817-836 MAR 2003
Times Cited: 83
UC-eLinks

5. Kuiper HA, Kleter GA, Noteborn HPJM, et al.
Assessment of the food safety issues related to genetically modified foods
PLANT JOURNAL 27 (6): 503-528 SEP 2001
Times Cited: 72
UC-eLinks

6. Tolstikov VV, Fiehn O
Analysis of highly polar compounds of plant origin: Combination of hydrophilic interaction chromatography and electrospray ion trap mass spectrometry
ANALYTICAL BIOCHEMISTRY 301 (2): 298-307 FEB 15 2002
Times Cited: 66
UC-eLinks

7. Fiehn O
Combining genomics, metabolome analysis, and biochemical modelling to understand metabolic networks
COMPARATIVE AND FUNCTIONAL GENOMICS 2 (3): 155-168 JUN 2001
Times Cited: 49
UC-eLinks

8. Watkins SM, Reifsnyder PR, Pan H, et al.
Lipid metabolome-wide effects of the PPAR gamma agonist rosiglitazone
JOURNAL OF LIPID RESEARCH 43 (11): 1809-1817 NOV 2002
Times Cited: 47
UC-eLinks

9. Weckwerth W
Metabolomics in systems biology
ANNUAL REVIEW OF PLANT BIOLOGY 54: 669-689 2003
Times Cited: 46
UC-eLinks

10. van Ommen B, Stierum R
Nutrigenomics: exploiting systems biology in the nutrition and health arena
CURRENT OPINION IN BIOTECHNOLOGY 13 (5): 517-521 OCT 2002
Times Cited: 39
UC-eLinks