



**Сања Антонић**

Универзитетска библиотека "Светозар Марковић"

[antonic@unilib.bg.ac.rs](mailto:antonic@unilib.bg.ac.rs)

# **Електронски часописи и књиге: доступност и проналажење**



# ШИРИ ТЕКСТ КУРСА СЛОБОДНО ДОСТУПАН НА САЈТУ УНИВЕРЗИТЕТСКЕ БИБЛИОТЕКЕ

[http://www.unilib.bg.ac.rs/edukacija/Tekst\\_za\\_kurs\\_za\\_doktorante\\_2011.pdf](http://www.unilib.bg.ac.rs/edukacija/Tekst_za_kurs_za_doktorante_2011.pdf)

и на сајту КоБСОН-а

Београду

О нама | Услуге | Електронска издања | Препоручени линкови | Пројекти | Заједница библиотека | Едукација


## ВЕСТИ

### КоБСОН за све, библиометријски индикатори и Publish or Perish

Драги библиотекари, чланови Заједнице библиотека универзитета у Србији, у току је одржавање радионица КоБСОН за све, библиометријски индикатори и Publish or Perish. Више информација можете видети у презентацији...

### ОБУКА КОРИСНИКА СРЕДОМ ОД 12 ДО 13 ЧАСОВА

Библиотека сваке среде, на спрату у главном холу, организује обуку корисника. Заинтересовани могу да се пријаве Одељењу за научне информације и едукацију путем електронске поште [edukacija@unilib.bg.ac.rs](mailto:edukacija@unilib.bg.ac.rs). Обуку могу да прате и корисници који нису пријављени. Циљ обуке је упознавање са услугама Библиотеке и са могућностима претраживања доступних извора информација (садржај обуке).  
Добродошле су све сугестије корисника!



Архива

Др Стела Филипи-Матутиновић : "Научне информације у Србији"

Универзитетска библиотека "Светозар Марковић" организује едукацију докторанада и млађих истраживача у области евалуације, приступа и коришћења електронских извора научних информација. Вишегодишње искуство стечено у интерактивном раду са полазницима ових курсева сабрано је у приручнику

Др Стела Филипи-Матутиновић : "Електронски извори информација у науци: значај, врсте, доступност, процена вредности"

Lynne Christine Alice - превела Србислава Маја Шаховић "Како написати предлог квалитативног истраживања"

Превод текста објављујемо уз сагласност издавача, Београдске отворене школе

Ashworth, Lucian M. - превела Србислава Маја Шаховић "Плагијаризам!"

Превод текста објављујемо уз сагласност издавача, Београдске отворене школе

Последњи пут промењено: 23/05/2012 7:47

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Булевар краља Александра 71, Београд · тел: (+381.11) 3370-509 · факс: (+381.11) 3370-354



# План

- Начини претраге
- Кобсонова страница
- Појединачни сервиси
- Ембарго, у штампи, ПДФ формат
- Електронске књиге
- Сервис eVrary

# Комбинација кључних речи

- Обавезно је коришћење логичких оператора између појмова
- Размислите о кључним речима
- Комбинујте прво мањи број појмова, а после додајте још појмова



# Синтагма

- Уколико не укуцате логичке операторе, база ће то да схвати као синтагму. У неким базама су обавезни наводници за синтагму
- Ако нисте сигурни да је ваш појам синтагма, убаците између речи логичке операторе

KoBSON

O Konzorcijumu

Načini pristupa

Vesti - arhiva

Statistike

Predavanja

Objavljeno o nama

Kako smo rasli

O eIFL-u

INFORMACIJE

NAUKA U SRBIJI

SERVISI

MOŽDA VAM ZATREBA

SUGESTIJE I ZAMERKE

## O Konzorcijumu

### O konzorcijumu

Konzorcijum biblioteka Srbije za objedinjenu nabavku (KoBSON) je novi oblik organizovanja biblioteka Srbije. Inicijativu za formiranje Konzorcijuma su pokrenule novembra 2001. vodeće naučne biblioteke u Srbiji:

- [Narodna biblioteka Srbije - Beograd](#)
- [Biblioteka Matice srpske - Novi Sad](#)
- [Univerzitetska biblioteke "Svetozar Marković" - Beograd](#)
- [Univerzitetska biblioteke "Nikola Tesla"- Niš](#)
- [Univerzitetska biblioteke - Kragujevac](#)
- [Biblioteka SANU - Beograd](#)
- [Zajednica univerzitetskih biblioteka](#)

Osnovni ciljevi udruživanja su:

- optimizovana nabavka stranih naučnih informacija
- prelazak sa papirnih izdanja na elektronska
- unapređenje pristupa elektronskim informacijama
- promocija domaćeg naučnog izdavaštva

Za predstavnika u pregovorima, kako sa izdavačima tako i sa nadležnim Ministarstvom određena je [Narodna biblioteka Srbije](#).

CPT

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EleČas

EleKnjige

Naši u WOS

Pomoć

Impresum

KoBSON

INFORMACIJE

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SERVISI

Pretraživanje časopisa

Elektronski časopisi

Pretraživanje knjiga

Elektronske knjige

Indeksne baze

Strane doktorske disertacije

Časopisi u papiru

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Servisi

## Servisi

U 2011. godini, iz akademskih institucija u Srbiji, dostupno je preko 35.000 naslova stranih naučnih časopisa u punom tekstu, oko 60.000 naslova knjiga, kao i nekoliko indeksnih baza podataka.

Pretraživanje na KoBSON portalu moguće je obaviti samo prema naslovu časopisa ili knjige. Većina časopisa je u punom tekstu je dostupna od 1997. godine, dok su ranija godišta dostupna do nivoa abstrakta.

Za predmetna pretraživanja po člancima upućujemo Vas ili na nekog od agregatora, ili direktno na sajt izdavača.

### Pretraživanje časopisa:

Spisak svih časopisa koji su na neki način dostupni u bibliotekama Srbije (bilo elektronski, bilo u papirnoj formi), proširena naslovima časopisa koji su imali Impakt Faktor u poslednjih dvadeset godina. Prisustvo časopisa na toj listi je samo pokazatelj njegove dostupnosti, a nikako kvaliteta.

### Elektronski časopisi:



IP: 147.91.1.41, RCUB



Početak / KoBSON / **Dobrodošli u KoBSON** /

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EleČas EleKnjige Naši u WOS Pomoć

Impresum



- KoBSON
- O Konzorcijumu
- Načini pristupa
- Vesti - arhiva
- Statistike
- Predavanja
- Objavljeno o nama
- Kako smo rasli
- O eIFL-u

- INFORMACIJE
- NAUKA U SRBIJI
- SERVISI
- MOŽDA VAM ZATREBA
- SUGESTIJE I ZAMERKE

## Dobrodošli u KoBSON

### Nova godina je počela u Naši u WoS

Sudeći prema podacima u WoS istraživačka 2013. je već počela. Ove nedelje prva četiri rada koja su napisali istraživači iz Srbije su dostupna u servisu Naši u WoS. Koristimo priliku da vam prvi čestitamo Novu godinu.

Vaš KoBSON

*(objavljeno 31.10.2012.)*

### Nedelja otvorenog pristupa (OA – Open Access) na Univerzitetu u Beogradu 22 - 28. oktobar 2012.

U organizaciji Univerzitetske biblioteke "Svetozar Marković" i partnerskih institucija od 22. do 28. oktobra 2012. godine na Univerzitetu u Beogradu u okviru Međunarodne nedelje otvorenog pristupa (OA Week) biće organizovan niz aktivnosti na promociji principa otvorenog pristupa naučnim informacijama.

**Program**

*(objavljeno 18.10.2012.)*

### Korekcija Impakt faktora za 2011

Baza EleČas je ažurirana novim vrednostima Impakt Faktora (IF) i pozicijama časopisa. Korekcija je izvršena na osnovu ispravki i dopuna koje je Thomson Reuters izvršio i publikovao u svojoj bazi Journal Citation Report (JCR).

- NOVI KORISNICI
- Ko ima pravo pristupa
- Kome je KoBSON dostupan
- KAKO KORISTITI KoBSON
- Pretraživanje časopisa
- Pretraživanje Naši u WoS
- Kako 'od kuće' do KoBSON-a
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- KoBSON ZA POČETNIKE
- ČESTA PITANJA O:
- Dostupnosti KoBSON-a
- Naši u WoS
- Našim časopisima
- Citiranosti autora
- SKRAĆENICE NA KoBSONu
- DoiSerbia
- Scindeks
- Google Schollar

## Pristup od "kuće"

Kompletan pristup KoBSON servisu moguć je i preko komercijalnih provajdera (ADSL, kablovski, dial-up i sl.). Jedini dopunski zahtev sastoji se u tome da korisnik **potpiše licencu** kojom se obavezuje da će se pridržavati pravila korišćenja. Pravo na ličnu licencu imaju svi **zaposleni u akademskim i naučnim institucijama čiji je osnivač Republika Srbija**, kao i **stipendisti Ministarstva nauke**. Dobijanje licence je besplatno.

Popunjena i potpisana Licenca, predaje se Centru za naučne informacije Narodne biblioteke Srbije ili bibliotekaru institucije u kojoj je istraživač zaposlen. Kako se prilikom podnošenja zahteva za pristup KoBSON servisima ne zahteva nikakva potvrda o zaposlenju, bibliotekar je taj koji garantuje da je korisnik zaista zaposlen u određenoj instituciji. Bibliotekar će zahtev proslediti nama putem **e-maila**, i nalog će biti otvoren istog dana. Istovremeno će korisniku biti upućen i e-mail sa podacima o dodeljenom korisničkom imenu i lozinki, kao i kratko uputstvo za korišćenje servisa. Nakon toga, prijavljivanje možete obaviti izborom opcije Udaljeni pristup u desnom gornjem uglu ekrana.





NALOG ZA OTVARANJE LIČNOG KORISNIČKOG IMENA  
NA SERVERU NARODNE BIBLIOTEKE SRBIJE

Molimo Vas da pažljivo pročitate sledeću licencu u kojoj su navedena pravila korišćenja Vašeg naloga.

Pre upotrebe svog naloga u Narodnoj biblioteci Srbije potvrđujem sledeće:

- ❖ Ja sam u ovom trenutku zaposlen/a u instituciji čiji je osnivač Republika Srbija.
- ❖ Preuzete članke ću koristiti samo za svoj vlastiti akademski rad radi dostizanja naučnog zvanja, podučavanja studenata, ili u istraživanjima koja finansiraju vlada ili neprofitne organizacije, a koja su namenjena objavljivanju u javno dostupnoj literaturi.
- ❖ NEĆU PREUZIMATI na svoj računar celokupne sveske časopisa (puni tekst časopisa, od korica do korica), jer je to protivno potpisanoj licenci.
- ❖ NEĆU KORISTITI preuzete članke za komercijalna istraživanja, npr. za istraživanja koja se sprovode u okviru konsultantskih ugovora i čiji se rezultati dostavljaju profitnim organizacijama, ili za istraživanja koja mogu dovesti do patenta.
- ❖ Koristiću rezultate pretraga u skladu sa uobičajenom praksom za akademska istraživanja, i poznato mi je da ih mogu čuvati u elektronskoj formi. Rezultate pretraživanja mogu da delim sa kolegama na ograničen i razuman način.
- ❖ Poznato mi je da se registruje svaki pristup elektronskim servisima preko ovog naloga, i da će ti podaci biti korišćeni samo za zbirno praćenje korišćenja elektronskih izvora.
- ❖ Poznato mi je da će mi pristup elektronskim servisima biti onemogućen, ukoliko svoj nalog budem koristio/la suprotno navedenim pravilima.
- ❖ Poznato mi je da je Licenca za upotrebu baza važeća na teritoriji Republike Srbije, i da kršenje licence od strane bilo kog korisnika može dovesti do raskida ugovora za sve korisnike iz Srbije.

Lični podaci:

Prezime, srednje slovo i ime	
Zvanje (npr. docent i sl., istraživač saradnik i sl., lekar)	
Institucija	
Grad	
e-mail adresa (ČITLJIVO)	
JMBG	

**Potpis**

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IP: 147.91.1.44, RCUB



Početak / SERVISI / **Elektronski časopisi** /

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EleČas Elektnjige Naši u WOS Pomoć

Impresum

- KoBSON
- INFORMACIJE
- NAUKA U SRBIJI
- SERVISI
- Pretraživanje časopisa
- Elektronski časopisi
- American Chemical Society
- American Physical Society
- ASME Transaction Journals
- EBSCO
- Caim.info
- Cambridge University Press
- Emerald
- Free medical Journals
- HeinOnline
- HINARI
- HighWire Press
- IEEE Computer
- Institute of Physics
- JSTOR
- Ovid
- Oxford Journals
- Project MUSE
- ProQuest
- Royal Society of Chemistry
- SAGE
- ScienceDirect
- Springer-Link
- TEEAL

### Elektronski časopisi

Kod većine izdavača KoBSON pretplađuje časopise u punom tekstu od 1997. godine, dok su ranija godišta dostupna do nivoa apstrakta. Predmetna, ili autorska, pretraživanja po člancima, moguće je obaviti:

- (1) na veb stranici izdavača izabranog iz menija, korišćenjem opcije brzo pretraživanje
- (2) na veb stranici izdavača
- (3) na veb stranicama agregatora (EBSCO, ProQuest)
- (4) indeksne baze (Web of Science, Scopus, Scindeks)

#### Elektronski časopisi:

Skup pretplaćenih izdavača čiji su naslovi dostupni u formi punog teksta.

Izdavači:

AC	American Chemical Society
AP	American Institute of Physics
ME	ASME Transaction Journals
CU	Cambridge University Press
EM	Emerald Publishing
IE	IEEE Digital Library
IO	Institute of Physics Publishing
OX	Oxford University Press
RC	Royal Society of Chemistry
SG	SAGE Pubishing
SD	Science Direct
SP	Springer/Kluwer
WI	Wiley Interscience

@ ☎

- NOVI KORISNICI
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- Citiranosti autora
- SKRAĆENICE NA KoBSONU
- DoiSerbia
- Scindeks
- Google Scholar
- Brza stranica



Ова страница је на језику: Хрватски ▾

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Преведи

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Опције ▾



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- [SAGE](#)
- [ScienceDirect](#)
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- [Pretraživanje knjiga](#)
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- [Indeksne baze](#)
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- [MOŽDA VAM ZATREBA ▶](#)
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Прешли сте на режим целог екрана. [Изађи из режима пуног екрана \(F11\)](#)

<b>AP</b>	ASME Transaction Journals
<b>ME</b>	Cambridge University Press
<b>CU</b>	Emerald Publishing
<b>EM</b>	IEEE Digital Library
<b>IE</b>	Institute of Physics Publishing
<b>IO</b>	Oxford University Press
<b>OX</b>	Royal Society of Chemistry
<b>RC</b>	SAGE Pubishing
<b>SG</b>	Science Direct
<b>SD</b>	Springer/Kluwer
<b>SP</b>	Wiley Interscience
<b>WI</b>	

- [SKRAĆENICE NA KoBSONu ▶](#)
- [DoiSerbia ▶](#)
- [Scindeks ▶](#)
- [Google Schollar ▶](#)
- [Brza stranica ▶](#)

**Агрегатори** (dostupni sa embargom ili periodom zakašnjenja od tri meseca do godinu dana):

<b>CI</b>	Cairn.info
<b>EB</b>	EBSCO
<b>HE</b>	Hein On Line
<b>HW</b>	High Wire
<b>FM</b>	Free Medical
<b>HI</b>	HINARI Helth Interent Work
<b>JS</b>	JSTORE
<b>OA</b>	Open Access (DOAJ)
<b>oa</b>	Open Access Archives (dostupna samo starija godišta)
<b>OV</b>	Ovid
<b>MU</b>	Project MUSE
<b>PQ</b>	ProQuest
<b>TE</b>	TEEAL
<b>👤</b>	Scindeks





IP: 147.91.1.42, RCUB

Početak / [SERVISI](#) / **Pretraživanje časopisa**

CPH SRL

Elečas Ele

- KoBSON ▶
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  - Pretraživanje časopisa
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  - Pretraživanje knjiga
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  - Strane doktorske disertacije
  - Časopisi u papiru
- MOŽDA VAM ZATREBA ▶
- SUGESTIJE I ZAMERKE ▶

### Pretraživanje časopisa

#### KoBSON lista

Spisak svih časopisa koji su na neki način dostupni u bibliotekama Srbije (bilo elektronski, bilo u papirnoj formi). Prisustvo časopisa na toj listi je samo pokazatelj njegove dostupnosti, a nikako kvaliteta.

#### Važno

Zabranjeno je preuzimanje svih radova iz jedne sveske časopisa (od korica do korica) jer bi to moglo dovesti do ukidanja pristupa tom servisu celoj akademskoj zajednici Srbije.

#### Časopisi u papirnoj formi

Za strane časopise koji se nalaze u bibliotekama Srbije čija su godišta navedena u određenom vremenskom opsegu, molimo da konsultujete biblioteke telefonom da bi proverili tačnu godinu, volumen i broj.

#### Nazivi disciplina

Nazivi Kategorija predstavljaju nazive disciplina, date su na

- izaberite oblast
- Acoustics
- Aerospace Engineering & Technology (current - Engineering, Aerospace)
- Agricultural Economics & Policy**
- Agricultural Engineering
- Agricultural Experiment Station Reports (current - Agricultural...)
- Agriculture (current - Agronomy)
- Agriculture, Dairy & Animal Science
- Agriculture, Multidisciplinary
- Agronomy
- Allergy
- Anatomy & Morphology
- Andrology
- Anesthesiology
- Anthropology
- Archaeology (AHCi)
- Archeology
- Architecture (AHCi)
- Area Studies
- Art (AHCi)
- Asian Studies (AHCi)
- Astronomy & Astrophysics
- Audiology & Speech-language Pathology
- Automation & Control Systems
- Behavioral Sciences
- Biochemical Research Methods
- Biochemistry & Molecular Biology
- Biodiversity Conservation
- Biology
- Biology, Miscellaneous (current - relevant discipline)

Pretraživanje

oblast Agriculture, Multidisciplinary;

1-20 / 57 časopisa



ISSN	Naslov	Servisi	IF 2011	
0167-8809	Agriculture Ecosystems and Environment	TE SD	3.004	<a href="#">detalji</a>
0308-521X	Agricultural Systems	TE SD	2.899	<a href="#">detalji</a>
0021-8561	Journal of Agricultural and Food Chemistry	AC	2.823	<a href="#">detalji</a>
0003-4746	Annals of Applied Biology	TE WI	2.179	<a href="#">detalji</a>
0021-8596	Journal of Agricultural Science	CU PQ	2.041	<a href="#">detalji</a>
0168-1699	Computers and Electronics in Agriculture	SD	1.846	<a href="#">detalji</a>
1473-5903	International Journal of Agricultural Sustainability	PQ	1.696	<a href="#">detalji</a>
1385-2256	Precision Agriculture	PQ SP	1.549	<a href="#">detalji</a>
0889-048X	Agriculture and Human Values	PQ SP	1.540	<a href="#">detalji</a>
0022-5142	Journal of the Science of Food and Agriculture	WI	1.436	<a href="#">detalji</a>
1836-0947	Crop & Pasture Science	TE	1.418	<a href="#">detalji</a>
1742-1705	Renewable Agriculture and Food Systems	CU PQ	1.274	<a href="#">detalji</a>
1187-7863	Journal of Agricultural and Environmental Ethics	PQ SP	1.109	<a href="#">detalji</a>
0791-6833	Irish Journal of Agricultural and Food Research		1.000	<a href="#">detalji</a>
1836-0939	Animal Production Science	TE	0.986	<a href="#">detalji</a>
1573-5214	Wageningen Journal of Life Sciences = Netherlands Journal of Agricultural Sciences / NJAS	TE SD	0.960	<a href="#">detalji</a>
1560-8530	International Journal of Agriculture and Biology	OA	0.940	<a href="#">detalji</a>
1459-6067	Agricultural and Food Science	OA	0.923	<a href="#">detalji</a>
0103-9016	Scientia Agricola	OA	0.864	<a href="#">detalji</a>
0028-8233	New Zealand Journal of Agricultural Research		0.853	<a href="#">detalji</a>



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Tražite

Udaljeni pristup

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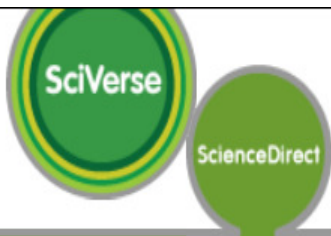
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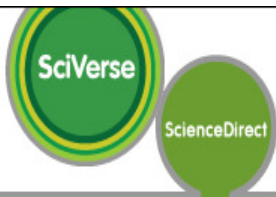
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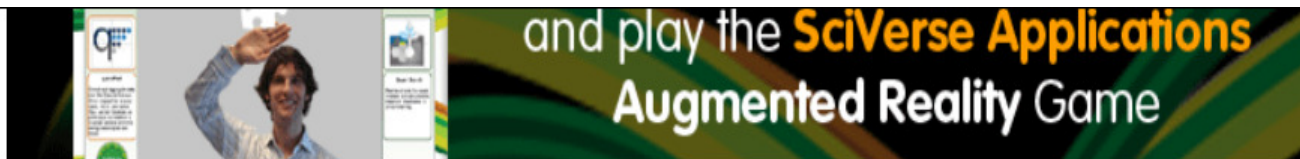


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#### Review

# Technical, bioinformatical and statistical aspects of liquid chromatography–mass spectrometry (LC–MS) and capillary electrophoresis–mass spectrometry (CE-MS) based clinical proteomics: A critical assessment

Mohammed Dakna<sup>a</sup>, Zengyou He<sup>b</sup>, Wei Chuan Yu<sup>b</sup>, Harald Mischak<sup>a</sup>, Walter Kolch<sup>c</sup>

<sup>a</sup> Mosaiques Diagnostics & Therapeutics, Hannover, Germany

<sup>b</sup> Department of Electronic and Computer Engineering, The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong, China

<sup>c</sup> The Beatson Institute for Cancer Research & Sir Henry Wellcome Functional Genomics Facility, University of Glasgow, Glasgow, UK

Received 9 July 2008; Accepted 28 October 2008. Available online 6 November 2008.

#### Abstract

The search for **biomarkers** in biological fluids that can be used for disease diagnosis and prognosis using mass spectrometry has emerged to become a state-of-the-art methodology for clinical proteomics. Poor cross platform comparison of the findings, however, makes the need for comparison studies probably as urgent as the need for new ones. It is now increasingly recognized that standardized statistical and bioinformatics approaches during data processing are of utmost importance for such comparisons. This paper reviews two of the currently most promising methods, namely LC–MS and CE-MS techniques, and software tools used to analyze the huge amount of data they generate. We further review the statistical issues of feature selection and sample classification.

**Keywords:** LC–MS; CE-MS; **biomarkers**; Clinical proteomics; Statistical data analysis

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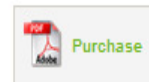
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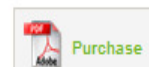


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#### Review

# Technical, bioinformatical and statistical aspects of liquid chromatography–mass spectrometry (LC–MS) and capillary electrophoresis–mass spectrometry (CE-MS) based clinical proteomics: A critical assessment

Mohammed Dakna<sup>a</sup>, Zengyou He<sup>b</sup>, Wei Chuan Yu<sup>b</sup>, Harald Mischak<sup>a</sup>, Walter Kolch<sup>c</sup>

<sup>a</sup> Mosaiques Diagnostics & Therapeutics, Hannover, Germany

<sup>b</sup> Department of Electronic and Computer Engineering, The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong, China

<sup>c</sup> The Beatson Institute for Cancer Research & Sir Henry Wellcome Functional Genomics Facility, University of Glasgow, Glasgow, UK

Received 9 July 2008; Accepted 28 October 2008. Available online 6 November 2008.

#### Abstract

The search for **biomarkers** in biological fluids that can be used for disease diagnosis and prognosis using mass spectrometry has emerged to become a state-of-the-art methodology for clinical proteomics. Poor cross platform comparison of the findings, however, makes the need for comparison studies probably as urgent as the need for new ones. It is now increasingly recognized that standardized statistical and bioinformatics approaches during data processing are of utmost importance for such comparisons. This paper reviews two of the currently most promising methods, namely LC–MS and CE-MS techniques, and software tools used to analyze the huge amount of data they generate. We further review the statistical issues of feature selection and sample classification.

**Keywords:** LC–MS; CE-MS; **biomarkers**; Clinical proteomics; Statistical data analysis

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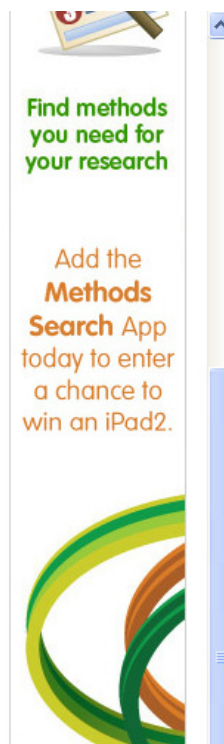
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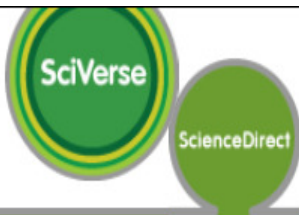
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<b>Naslov</b>	<b>STICS: a generic model for the simulation of crops and their water and nitrogen balances. I. Theory and parameterization applied to wheat and corn</b>
<b>Autor(i)</b>	<b>Brisson-N. Mary-B. Ripoche-D. Jeuffroy-M-H. Ruget-F. Nicoullaud-B. Gate-P. Devienne-Barret-F. Antonioletti-R. Durr-C. Richard-G. Beaudoin-N. Recous-S. Tayot-X. Plenet-D. Cellier-P. Machet-J-M. Meynard-J-M. Delecolle-R</b>
<b>Abstract</b>	<b>STICS (Simulateur multIdisciplinaire pour les Cultures Standard, generic multidisciplinary simulation model for crops) simulates crop yield and quality and environmental effects of crop husbandry, using data on climate, soil and agronomic practices. The seven modules of STICS (development, shoot growth, yield components, root growth, water balance, thermal environment and nitrogen balance) are each described with reference to wheat and maize, with a discussion about the theoretical choices in comparison with other models.</b>
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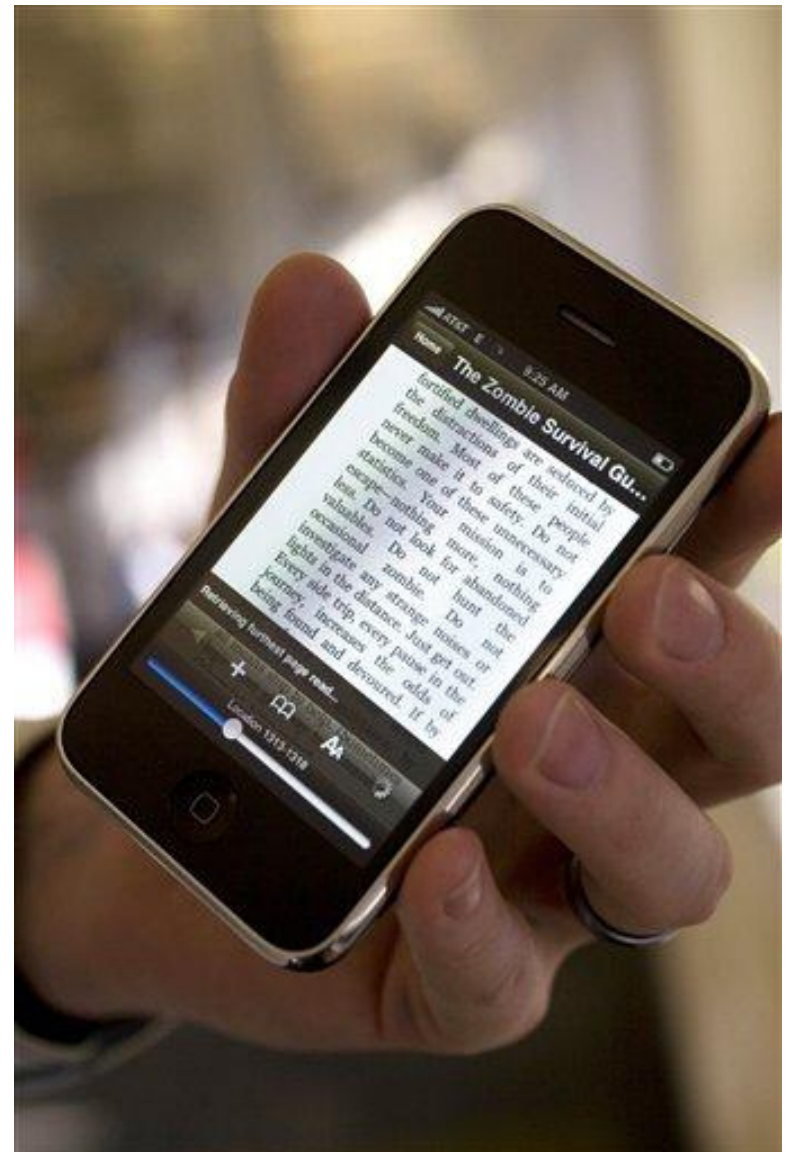
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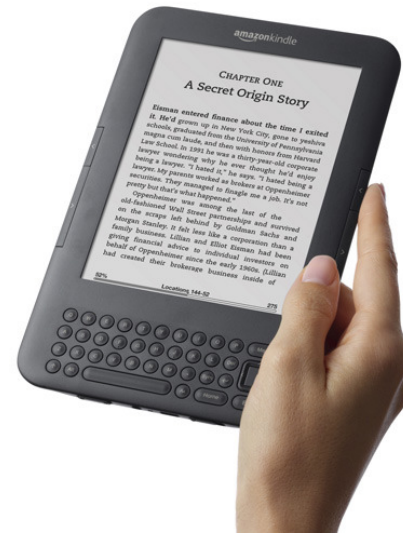
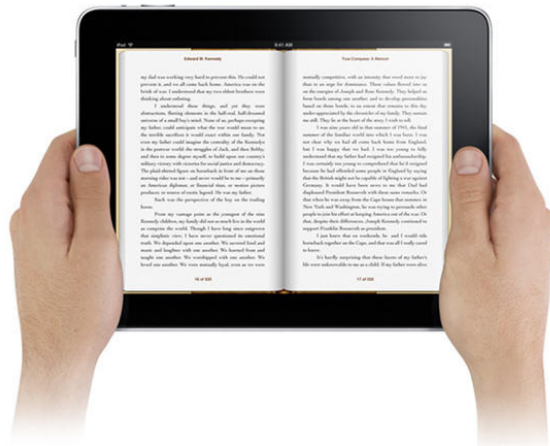
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## Biomedical Polymers and Polymer Therapeutics

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# PHARMACEUTICAL ASPECTS OF GENE THERAPY

Philip R. Dash and Leonard W. Seymour  
*CRC Institute for Cancer Studies, University of Birmingham, B15 2TA, U.K.*

## 1. INTRODUCTION

The concept of gene therapy as a treatment for human disease is almost as old as molecular biology itself. One of the first proposals for the use of genes in the treatment of human diseases was made by Tatum in his 1958 Nobel Prize acceptance speech, while the term gene therapy was coined by Szybalski in the early 1960s<sup>1</sup>. However, it wasn't until the early 1990s that the science of gene therapy had progressed enough to enter clinical trials<sup>2</sup>.

The idea underlying gene therapy is that human disease might be treated by the transfer of genetic material into specific cells of a patient in order either to replace a defective gene or to introduce a new function to the cell<sup>3,4</sup>. The potential of gene therapy to treat a wide range of diseases has led to very rapid advances in the science of gene transfer and in understanding the molecular basis of many diseases. Despite this and a



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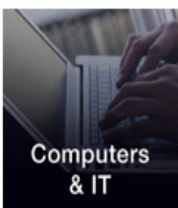
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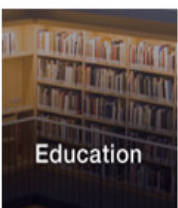
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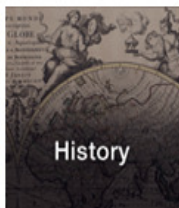
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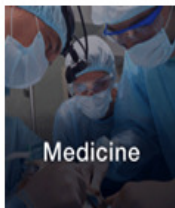
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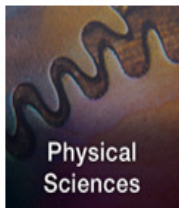
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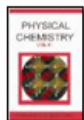
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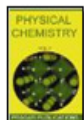
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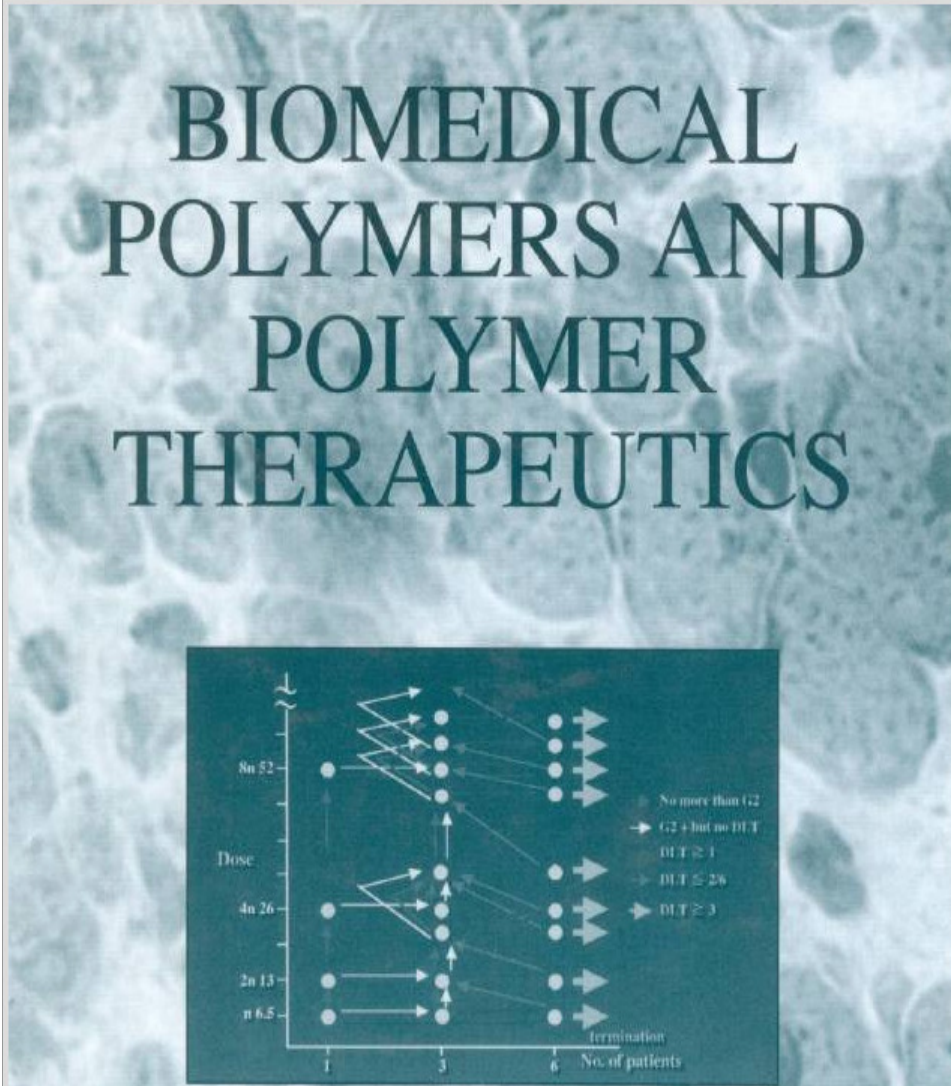
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*W.E. Hennink, J.A. Cadée, S.J. de Jong, O. Franssen, R.J.H. Stenekes, H. Talsma, and W.N.E. van Kijk-Wolthuis*

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### Chapter 1

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## POTENTIAL DISEASE TARGETS FOR GENE THERAPY

### 1.1 Gene therapy of inherited genetic diseases

The replacement of inherited defective genes is, perhaps, the most obvious use of gene therapy. The aim of replacement gene therapy is to replace a missing or defective gene that is responsible for the disease in order to restore normal function. The ultimate aim is the permanent correction of the disorder, possibly by integration of the gene into stem cells. A major limitation to this type of treatment is the problem of gaining access to the relevant tissues. For this reason, the early gene replacement strategies have focused on readily accessible tissue such as muscle, lung, blood and bone marrow<sup>3</sup>.

Blood cells and bone marrow are associated with a number of relatively

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## ESSENTIAL DISEASE TARGETS FOR GENE THERAPY

### 1.1 Gene therapy of inherited genetic diseases

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replace a missing or defective gene that is responsible for the disease in order to restore normal function. The ultimate aim is the permanent correction of the disorder, possibly by integration of the gene into stem cells. A major limitation to this type of treatment is the problem of gaining access to the relevant tissues. For this reason, the early gene replacement strategies have focused on readily accessible tissue such as muscle, lung, blood and bone marrow<sup>3</sup>.

Blood cells and bone marrow are associated with a number of relatively common genetic diseases and as such are a major target for gene therapy. Gene transfer into lymphocytes or haemopoetic stem cells potentially allows the treatment of a variety of diseases including immune deficiency disorders such as adenosine deaminase deficiency (ADA-SCID); storage disorders such as Gaucher's disease and haemoglobinopathies such as sickle cell anaemia and the thalasseмии. The only clinical trials involving gene transfer into lymphocytes have been concerned with the correction of ADA-SCID, a very rare immune deficiency syndrome, and most work has concentrated on transfer of genes into stem cells<sup>1</sup>.

Cystic fibrosis is the most common inherited genetic disease in Europe and the United States. A mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene results in the production of an abnormal protein that does not properly control the flow of chloride ions across membranes. The major clinical manifestation of this disease is in the airway epithelia, resulting in chronic inflammation with subsequent damage to the lung tissue. The average life expectancy of patients with CF is around 30



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Gene therapy has the potential to be used in the treatment of almost any disease with a genetic component. There are a number of cardiovascular diseases that are under investigation for possible treatment with gene therapy. For example, familial hypercholesterolaemia might be treated by transferring the gene encoding for the low density lipoprotein receptor into hepatocytes in order to reduce the level of serum cholesterol<sup>10-12</sup>. Other strategies for the gene therapy of cardiovascular disease include inhibiting smooth muscle cell proliferation, that might lead to stenosis, following balloon angioplasty<sup>13,14</sup> and stimulation of vascular growth to overcome ischaemia<sup>10</sup>.

Other diseases that have been investigated for possible treatment with gene therapy include AIDS<sup>1,15</sup>, neurodegenerative diseases such as Alzheimer's and Parkinson's<sup>16</sup>, traumatic nerve injury<sup>17</sup> and autoimmune diseases<sup>1,18</sup>.

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Other diseases that have been investigated for possible treatment with gene therapy include AIDS 1,15 , neurodegenerative diseases such as Alzheimer's and Parkinson's 16 , traumatic nerve injury 17 and autoimmune diseases 1,18 .

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or the gene therapy clinical trials .

There are numerous approaches to using gene therapy to treat cancer, and some of these are outlined below.

*Immunotherapy.* The immunotherapy approach to cancer gene therapy is one in which the immunogenicity of tumours is increased by causing the local production of immunomodulatory agents such as cytokines (interleukin-2 or granulocyte macrophage colony stimulating factor for example) or by increasing the level of MHC antigen expression<sup>7</sup>. Increasing the immunogenicity of tumours may then lead to an antitumour response. Because immunity is a systemic reaction, this immune reaction could potentially eliminate all the tumour cells in the body, including sites of metastatic deposit.

*Gene Directed Enzyme Pro-drug Therapy (GDEPT).* The introduction of genes that encode enzymes capable of converting pro-drugs to cytotoxic drugs is the basis of the GDEPT approach to cancer gene therapy. A relatively harmless pro-drug can be administered to a patient following the transfection of some tumour cells with genes encoding enzymes that will activate the pro-drug *in situ* to form a cytotoxic drug that will kill the tumour cell. This approach may be considered as using gene therapy to improve upon conventional chemotherapy. The local expression of an activating enzyme ensures that the peripheral toxicity often associated with chemotherapy is reduced. The use of a relatively harmless pro-drug ensures that high doses can be administered to the patient, resulting in high

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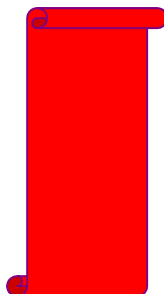
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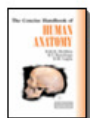
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replace a missing or defective gene that is responsible for the disease in order to restore normal function. The ultimate aim is the permanent correction of the disorder, possibly by integration of the gene into stem cells. A major limitation to this type of treatment is the problem of gaining access to the relevant tissues. For this reason, the early gene replacement strategies have focused on readily accessible tissue such as muscle, lung, blood and bone marrow<sup>3</sup>.

Blood cells and bone marrow are associated with a number of relatively common genetic diseases and as such are a major target for gene therapy. Gene transfer into lymphocytes or haemopoietic stem cells potentially allows the treatment of a variety of diseases including immune deficiency disorders such as adenosine deaminase deficiency (ADA-SCID); storage disorders such as Gaucher's disease and haemoglobinopathies such as sickle cell anaemia and the thalassemias. The only clinical trials involving gene transfer into lymphocytes have been concerned with the correction of ADA-SCID, a very rare immune deficiency syndrome, and most work has concentrated on transfer of genes into stem cells<sup>1</sup>.

Cystic fibrosis is the most common inherited genetic disease in Europe and the United States. A mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene results in the production of an abnormal protein that does not properly control the flow of chloride ions across membranes. The major clinical manifestation of this disease is in the airway epithelia, resulting in chronic inflammation with subsequent damage to the lung tissue. The average life expectancy of patients with CF is around 30

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