Personal experiences on patenting part II

Marc Baumann

Biomedicum Helsinki

FIN-00014 University of Helsinki

http://www.research.med.helsinki.fi\corefacilities\proteinchem

Where did it all began?

1992

The preparative gel electrophoresis story!

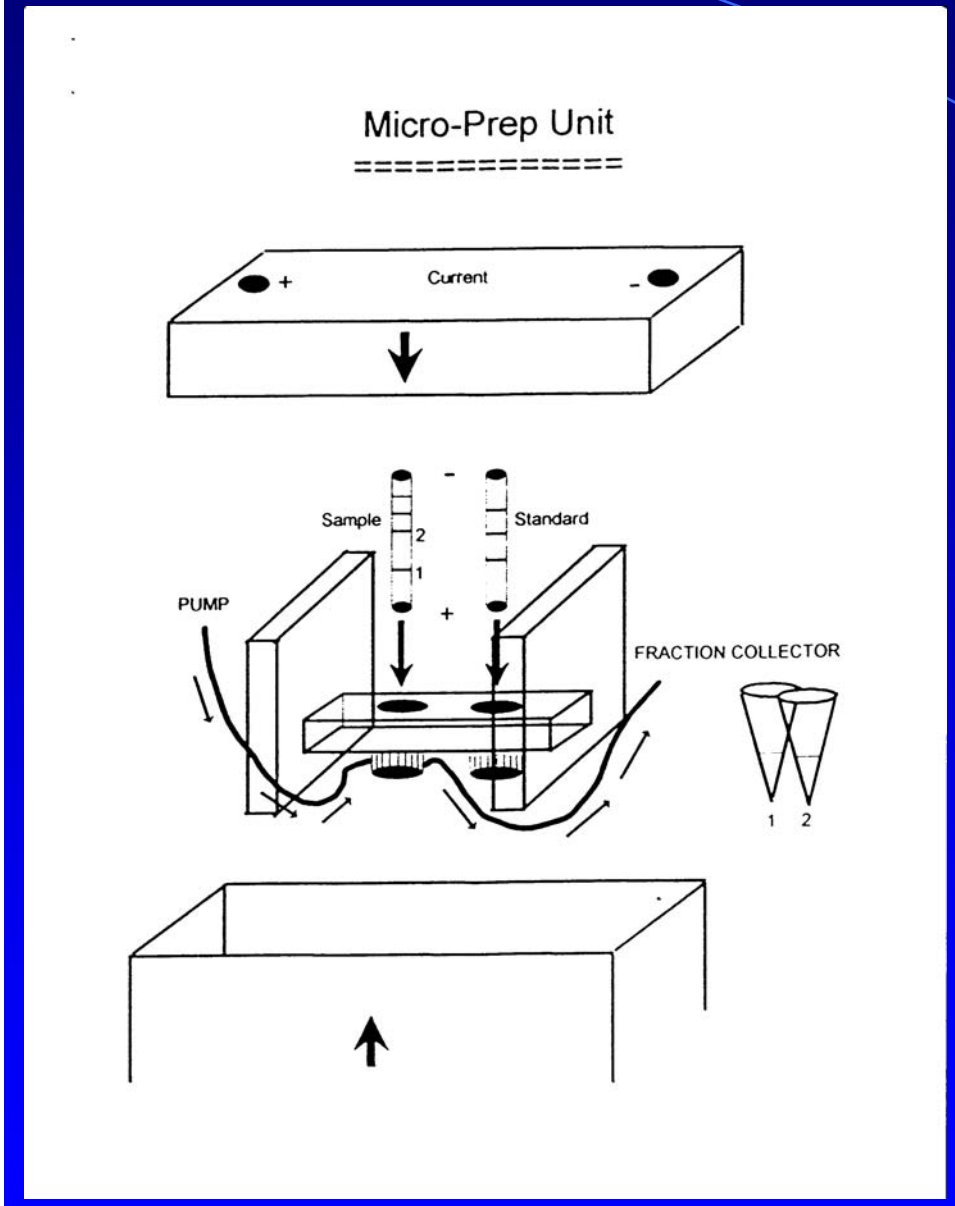
I was fed up with the existing technologies for protein purification and decided to…

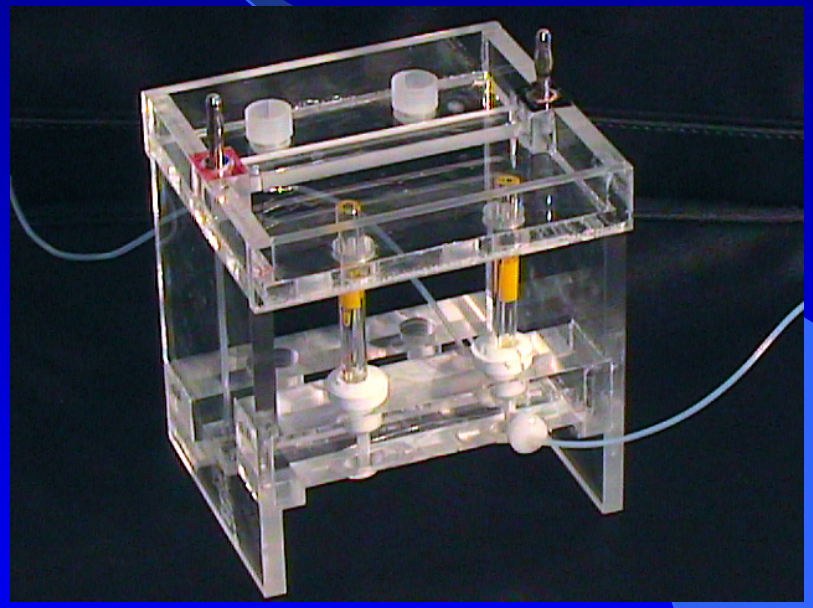
Make my own instruments for using electrophoresis in protein purification.

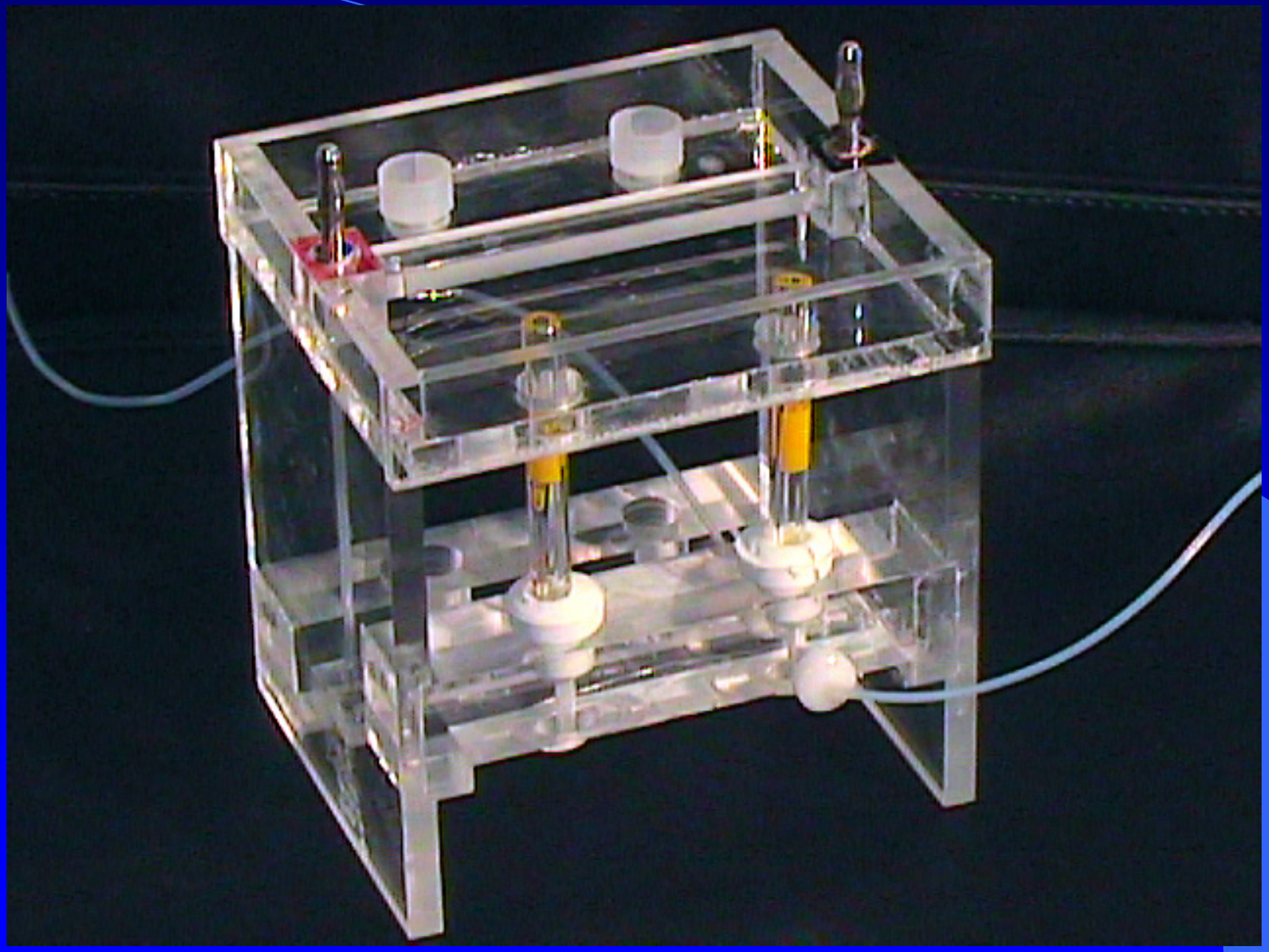
For that I needed:

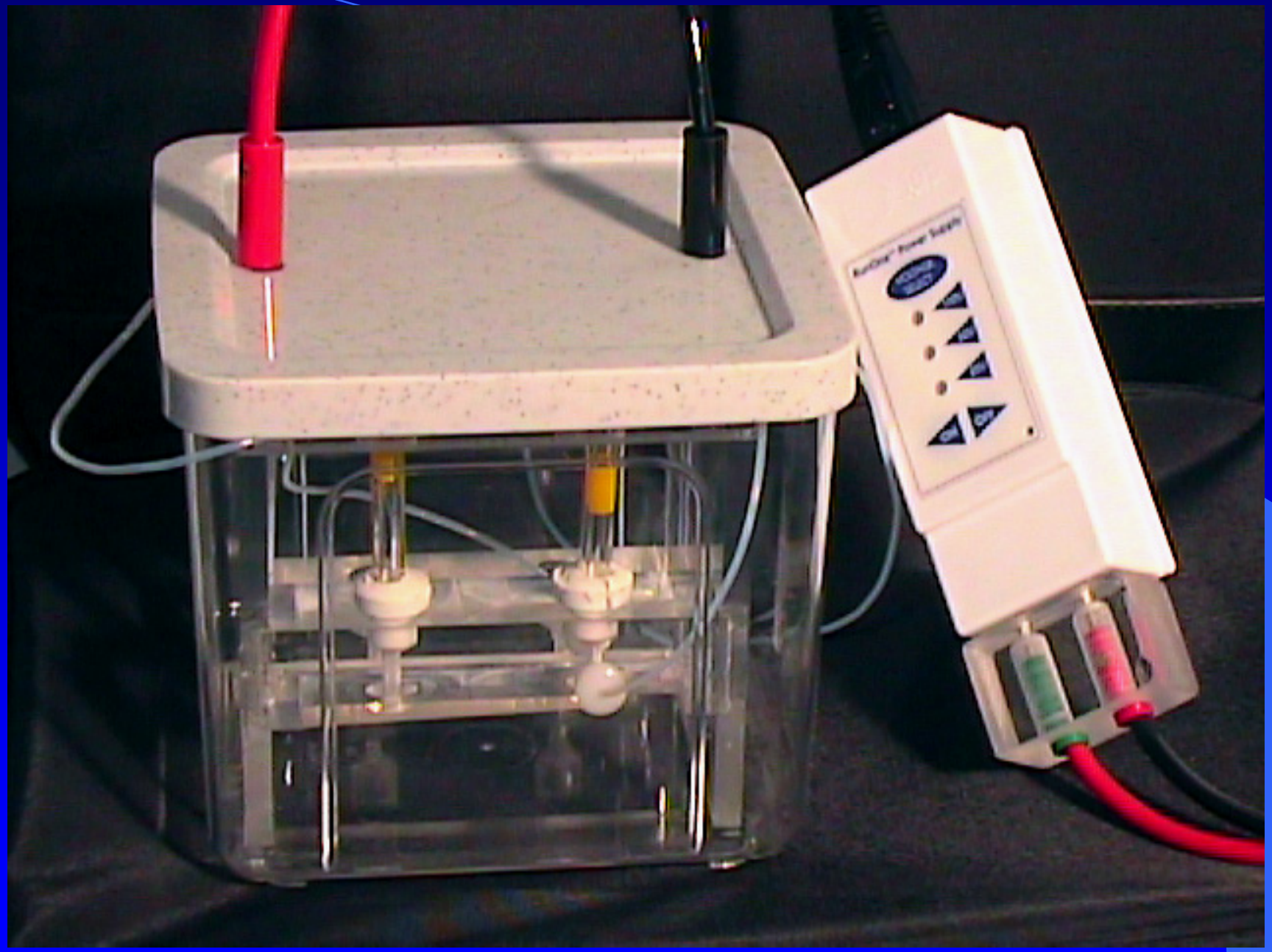
1) An idea
2) Money
3) Commercial education
4) A Company (or many?)

The Idea!


Micro-Prep Unit
==========
+
Current
-
Sample
Standard
2
1
-
+
PUMP
FRACTION COLLECTOR
1
2







Money or more products?

First collaboration with BioRad (BioRad is one of the largest biotechnology companies in the world!)

Mini-Prep Cell

Let’s go shortly to the BioRad www site…

So my machine was finally combined with a commercial device

Patents at this stage?

No patents filed = and everything went very smoothly
3 years coll. with full support

But what about money?

Where do you get money in Finland?

>> everywhere and nowhere…

Whom to contact?

University IPR office?

Licentia?

Helsinki Business and Science park?

TEKES?

Individual scientist?

- but whom?

Telephone operator …

I went to SPINNO

SPINNO is an education from the UH and TKK which want to support spin-off from academia

My first contract

KEKSINTÖSÄÄTIÖ

KEKSIJÄN RAHOITUSSOPIMUS N:o 97112504

1. OSAPUOLET

a) Rahoittajana Keksintösäätiö (jäljempänä Säätiö) ja

b) rahoituksen saajana Marc Baumann (jäljempänä Keksijä)
Pohj. Hesperiankatu 3 B 10
00260 HELSINKI
puh: (09) 443 818
fax:

2. SOPIMUKSEN TARKOITUS

Tämän sopimuksen ja liitteenä 2 olevien *Rahoitussopimuksen yleisten ehtojen* mukaisesti Säätiö rahoittaa Keksijän jäljempänä 3. kohdassa kuvatun keksinnön (jäljempänä Keksintö)

- patentointiin tai muuhun teollisoikeudelliseen suojaamiseen
- tuotekehitykseen
- markkinointiin tai
- muuhun keksinnön kehittämiseen

liittyviä toimenpiteitä 4. kohdan mukaisesti.

3. RAHOITUKSEN PERUSTEENA OLEVA KEKSINTÖ

Rahoitus perustuu Keksintöön, jonka nimi on ELEKTROFOREETTISIA ANALYYSILAITTEITA

Sopimuksen piiriin kuuluvat myös Keksintöön olennaisesti liittyvät jatkokeksinnöt sekä Keksinnön muutokset ja parannukset.

4. RAHOITUKSEN MÄÄRÄ JA NOSTAMINEN

Keksijälle on myönnetty liitteen 1 mukaisesti *Tukiraha,* jonka käyttäminen Keksinnön kehittämisestä aiheutuviin kustannuksiin on selvitetty samassa liitteessä. Arvonlisäverovelvollinen Keksijä saa Tukirahalla kattaa hyväksyttävien kustannusten arvonlisäveroa sisältämättömän osuuden.

Tukirahan määrän Keksijä saa nostaa erissä liitteenä 2 olevien *Rahoitussopimuksen yleisten ehtojen* mukaisesti. Edellytyksenä tukirahaerän maksamiselle Keksijälle tai erikseen sovittaessa hyväksyttävän kustannuksen velkojalle on joko maksupyyntö, jonka Säätiö on hyväksynyt tai muu Rahoitussopimuksen yleisten ehtojen mukainen maksatuksen hyväksyminen. Kutakin nostettavaa erää varten erikseen Keksijä tekee maksupyynnön liitteenä 3 olevalle *maksupyyntölomakkeelle.* Toisen erän ja sitä myöhempien erien nostamisen edellytyksenä on lisäksi Keksijän tekemä selvitys edellisen erän rahankäytöstä. Selvityksestä on käytävä ilmi maksun saaja ja maksun aihe sekä päivämäärä ja markkamäärä. Viimeisen erän käytöstä Keksijä antaa selvityksen vuosiraportissa (liite 4).

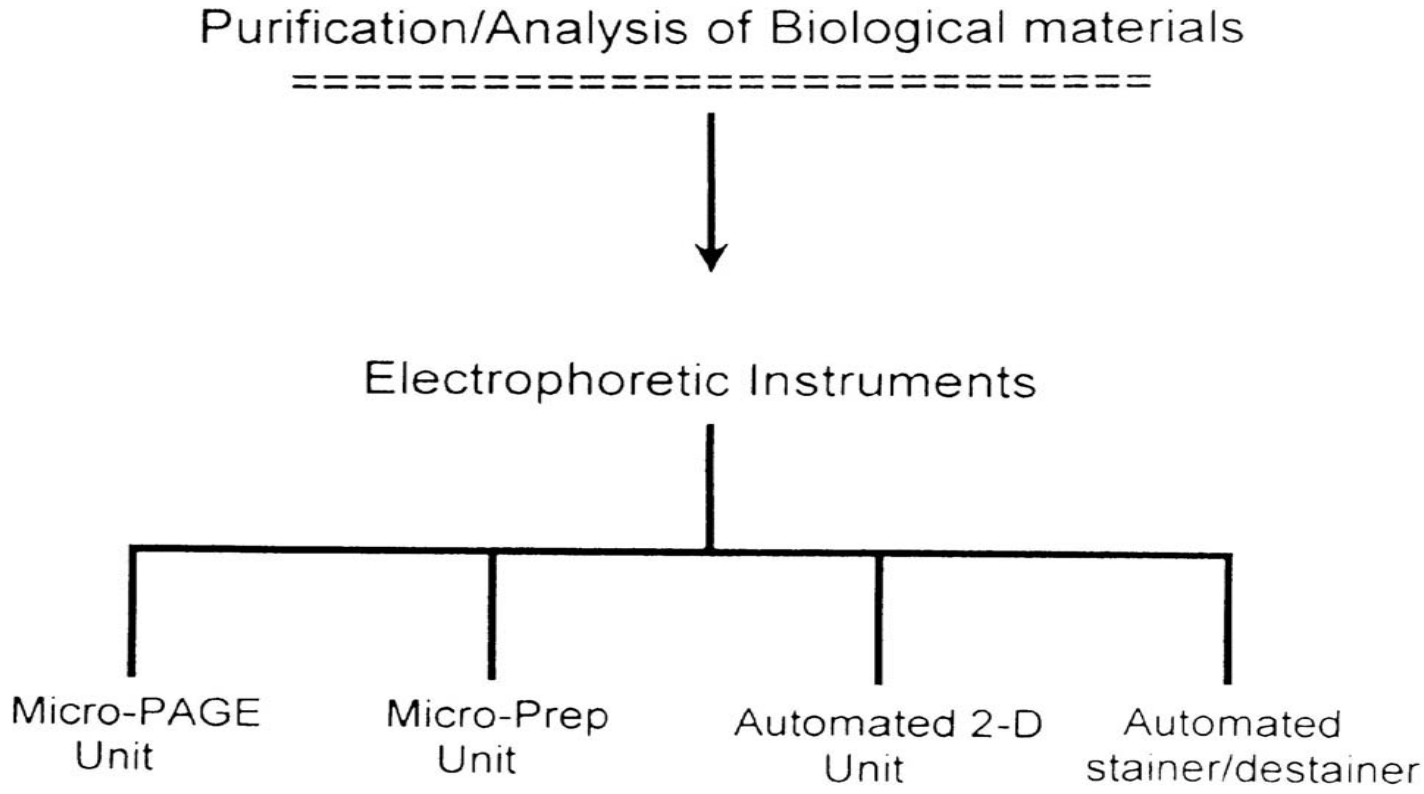
Tukiraha on Keksijän käytettävissä sopimuksen voimaantulosta lähtien voimaantulon kalenterivuotta seuraavan toisen kalenterivuoden marraskuun 30:nteen päivään asti. Keksijä menettää oikeutensa siihen

My first AWARD

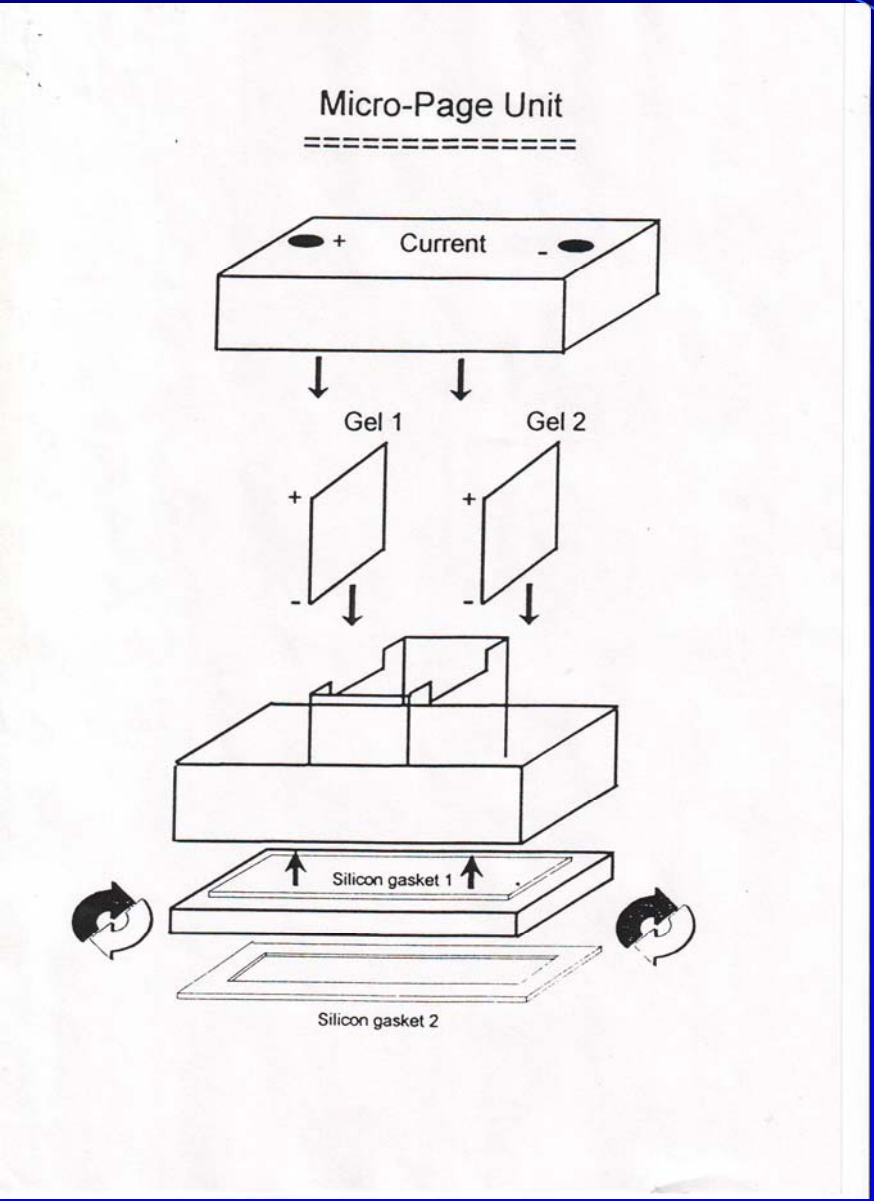
50.000

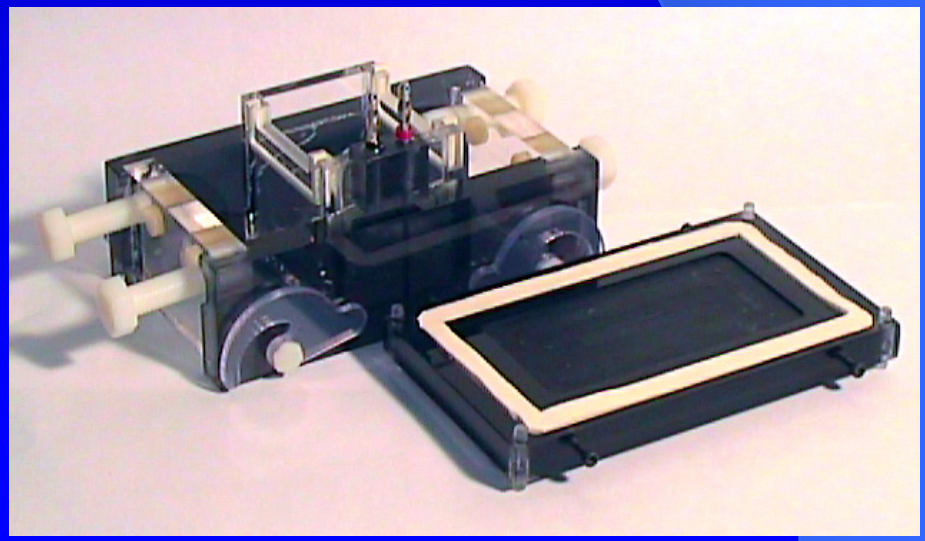
for a great invention
(still not a patent)

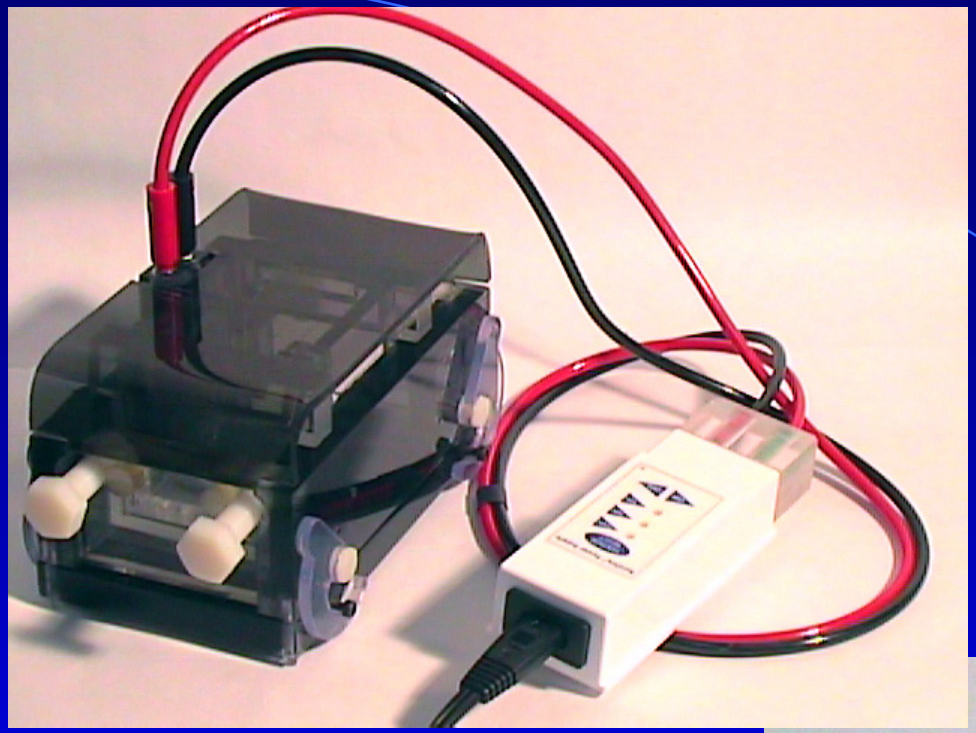
Development of new products

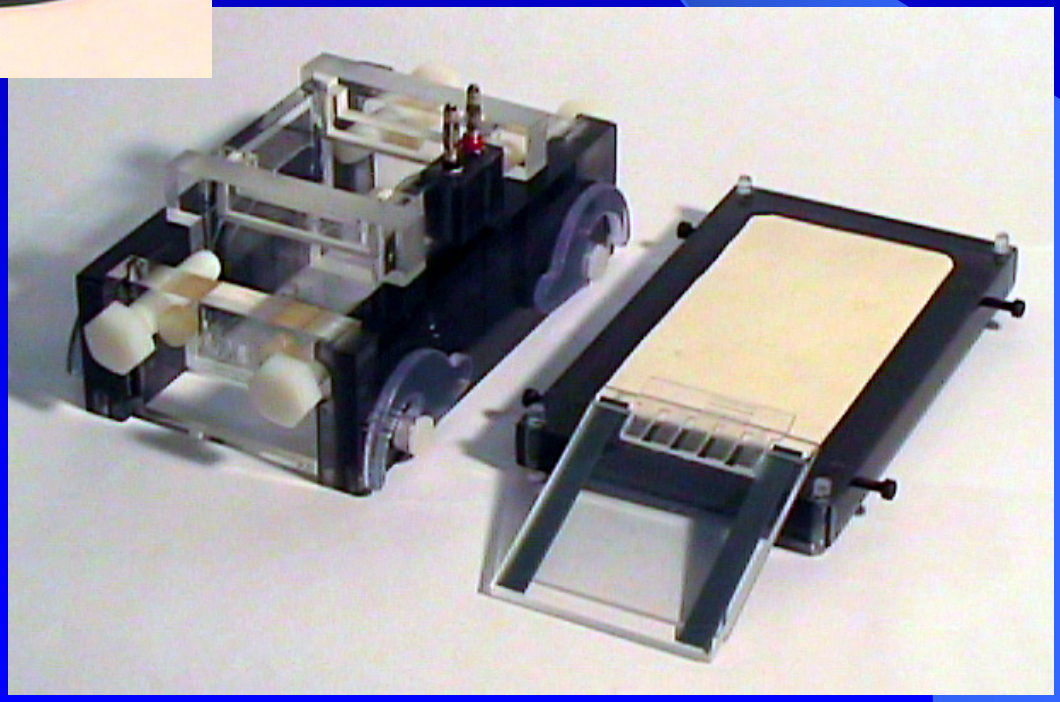


Development of new products

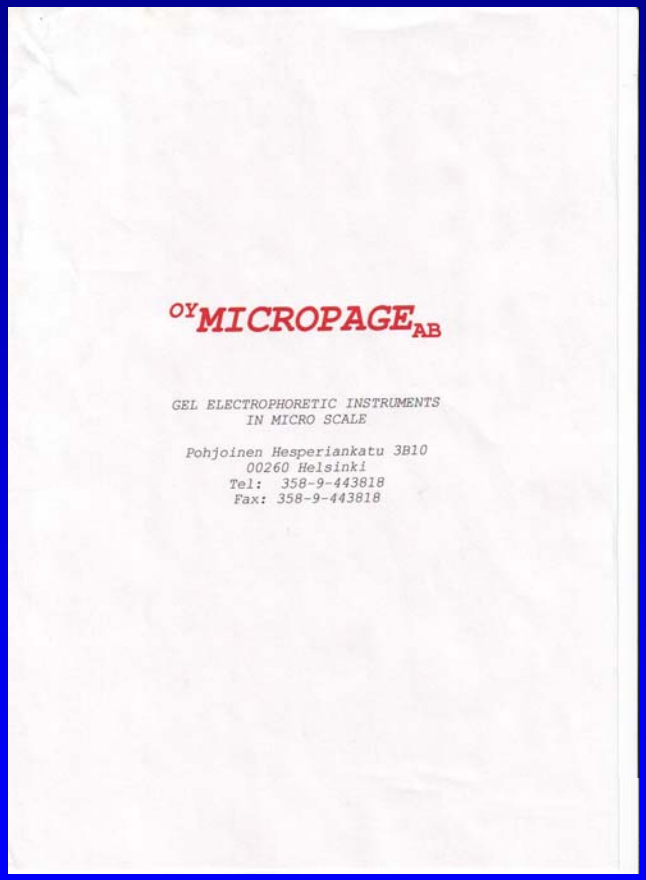








My first Company



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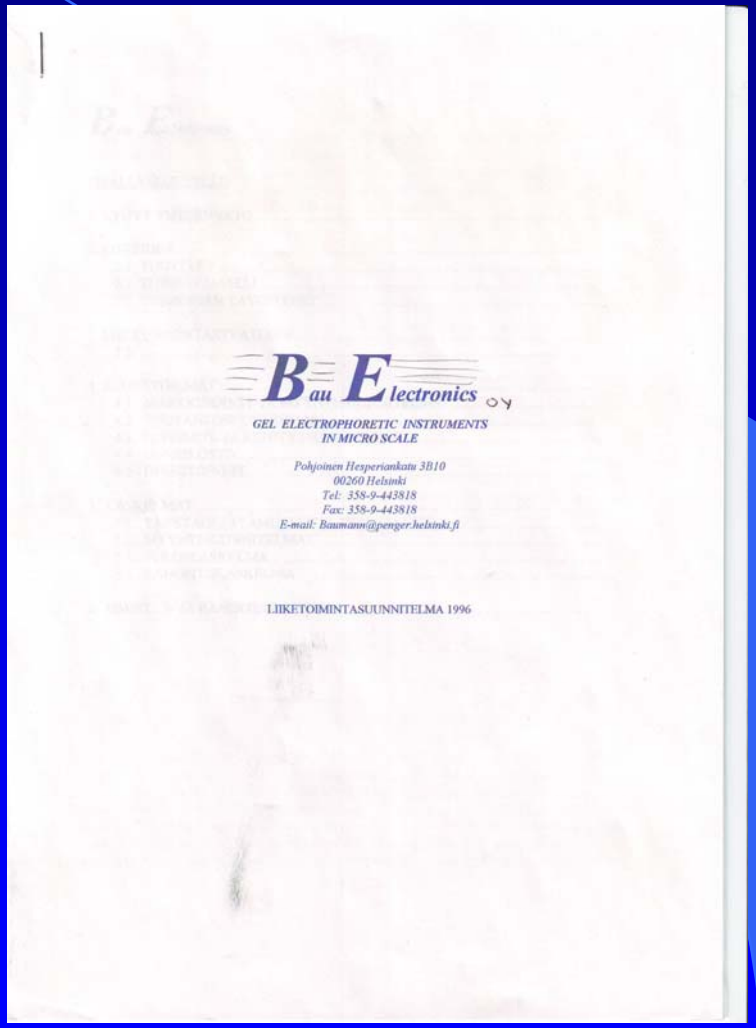


Microgel Biotechnologies ltd
Pohjoinen Hesperiankatu 3B10
00260 Helsinki 26
Finland
Tel: 09-443818 // 040-5148061
E-mail: Microgel@Megabaud.fi

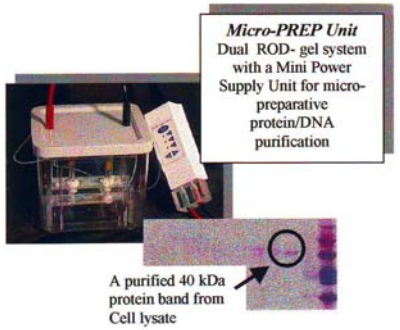
LEHDISTÖTIEDOTE Helsinki, 15.4.98

Microgel Biotechnologies ltd on uusi suomalainen yritys joka kehittää ja valmistaa elektroforeettisia analyysilaitteita ja niihin tarvittavia oheistuotteita bioteknologiseen tutkimukseen. Laitteet erottavat ja puhdistavat biomolekyylejä (valkuaisaineita, sekä DNA ja RNA molekyylejä) eri kantajamateriaaleissa kunkin komponentin ominaisvarauksen ja/tai massaeron avulla. Yrityksen tuotevalikoima kattaa ensivaiheessa kaikki tarvittavat komponentit täydellisen analyysi- ja/tai puhdistus toimenpiteen suorittamiseksi. Myöhemmin tuotevalikoimaan tullaan liitämään laitteita jotka voivat hyödyntää eri komponenttien varaus- ja massaeroja jopa saman suorituksen aikana, sekä laitteita jotka suoriutuvat kantajamateriaalien jälkikäsittelystä taysin automaattisesti. Microgel Biotec:n laitteet on suunniteltu erityisesti pienten näytemäärien käsittelyyn. Suunnittelussa on lisäksi kiinnitetty erityistä huomioita yleiseen kätevyyteen, käyttövarmuuteen sekä korkeaan laatuun.

Microgel Biotechnologies ltd

Go smart, Go small...

BioRunner Inc. provides You now with fast small size Gel electrophoresis Units to get the best out of YourTIME!



Micro-PREP Unit
Dual ROD- gel system with a Mini Power Supply Unit for micro-preparative protein/DNA purification

A purified 40 kDa protein band from Cell lysate

Micro-PAGE Unit
Analytical micro-scale electrophoresis Unit with the Casting and Running "All-in-One"-system

Running Gel Electrophoresis In Microscale

Why would You use a regular gel for just a quick check out?

Why would You use a 10-well gel just for a few samples?

You wouldn't if You had a choice !!!!

Biofellows Oy, Viikinkaari 6, 00710 Helsinki, puh. 09- 755 2550, faksi 09-755 255 55; www.biofellows.com

Bio Runner Inc., Pohjoinen Hesperiankatu 3B10, 00260 Helsinki, Finland
Tel. 040-5148061; E-Mail: biorunner@megabaud.fi

So I had lived a nice life with alot of excitement

Until one day a decided to go for

PATENTS

My first patent

Let’s check the PRH site…

A drug for Alzheimers diseases!

Now money comes in?

Filing a patent in the BIG Apple

NYU (New York University)

- no costs for the inventor
-no hassle for the inventor
-proper agreement with inventor
-great opportunity

Designing Drugs Inhibiting protein misfolding in Alzheimer's Disease, Amyloidoses and Prion Disorders

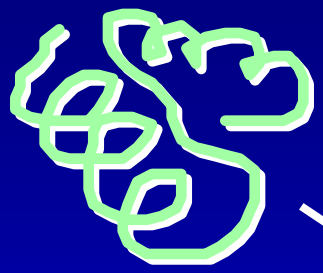
Marc Baumann

Protein Chemistry/Proteomics Unit
and the Neuroscience Program

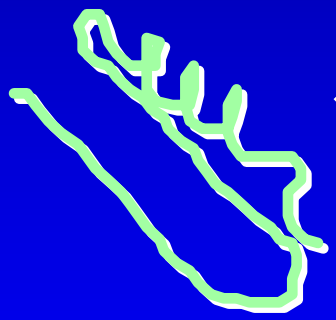
Biomedicum Helsinki

E-Mail: marc.baumann@helsinki.fi

Protein misfolding, what can it do?



Folded
functional protein



Non-folded
Non-functional protein

Conformational change

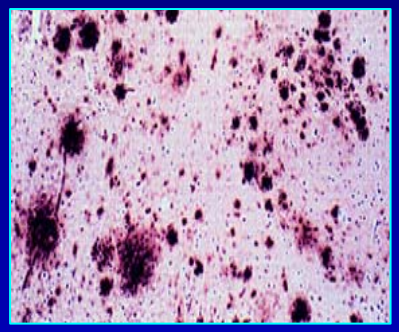
Abnormal protein

- Can cause a loss of the physiological function
- Can cause aggregation and deposition
- Can become toxic

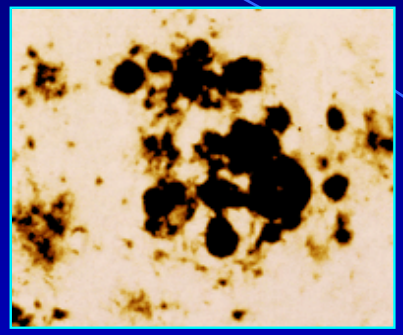
Examples of protein misfolding disorders

Disease	Protein involved
Alzheimer's disease,	Amyloid-ß protein
CJD, FFI , Kuru, BSE	Prion protein
Parkinson disease	α-synuclein, parkin (?)
Huntington disease	Huntingtin
Diabetes type II	Amylin
Amyotrophic lateral sclerosis	Superoxide dismutase
Serpin deficiency, emphysema, cirrhosis	Serpins
Haemodialysis amyloidosis, prostatic amyloid	ß2-microglobulin
Cystic fibrosis	CFTR protein
CADASIL disease	Notch3 receptor protein
Etc, etc, etc...	

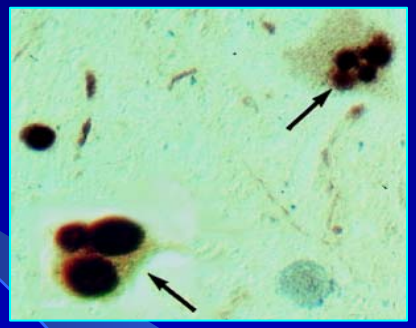
Protein Aggregates in Conformational Disorders



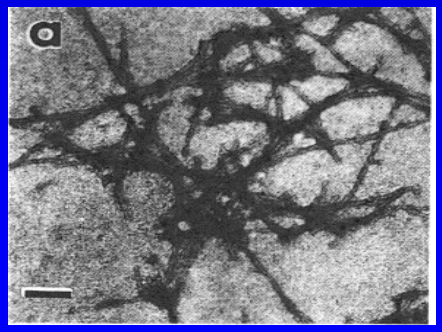
Alzheimer's amyloid plaques

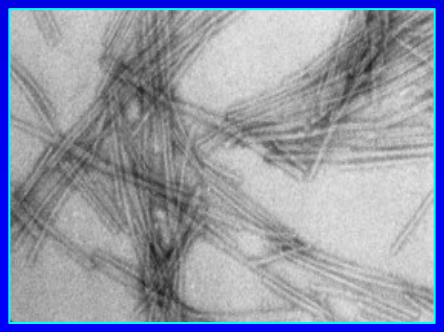


Prion plaques



Parkinson's Lewy bodies

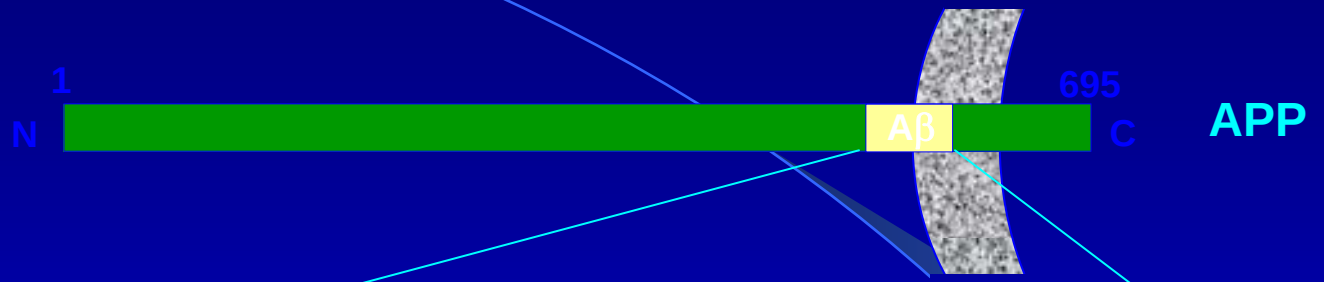




Amyloid fibers

Aggregates

Sequences of Alzheimer's β-sheet breaker peptides



Aβ1-42 DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGVVIA

1 42

β-sheet breaker peptides

iAβ11	RDLPFFPVPID
iAβ9	RDLPFFPVD
iAβ7	LPFFPVD
iAβ6	LPFFVD
iAβ5	LPFFD

Peptides and pharmaceutical compositions thereof for treatment of disorders or diseases associated with abnormal protein folding into amyloid or amyloid-like deposits

Patenttinumero:	US6462171
Julkaisupäivä:	2002-10-08
Keksijä(t):	SOTO-JARA CLAUDIO (CH); BAUMANN MARC H (FI); FRANGIONE BLAS (US)
Hakija(t):	UNIV NEW YORK (US)
Pyydetty patentti:	☐ US6462171
Hakemusnumero:	US19960766596 19961212
Prioriteettinumero(t):	US19960766596 19961212; US19960630645 19960410; US19950478326 19950607
IPC-luokitus	A61K38/00; C07K16/00
EC-luokitus	C07K14/47A3, G01N33/68V2, A61K49/00H6, C07K5/08H2A
Vastineet:	

Tiivistelmä

Novel peptides capable of interacting with a hydrophobic beta-sheet forming cluster of amino acid residues on a protein or peptide for amyloid or amyloid-like deposit formation inhibit and structurally block the abnormal folding of proteins and peptides into amyloid or amyloid-like deposits and into pathological beta-sheet-rich conformation as precursors thereof. Methods for preventing, treating or detecting disorders or diseases associated with amyloid-like fibril deposits, such as Alzheimer's disease and prion-related encephalopathies, are also provided

My second patent

Let’s check the PRH site…

Micro-chips for proteomics

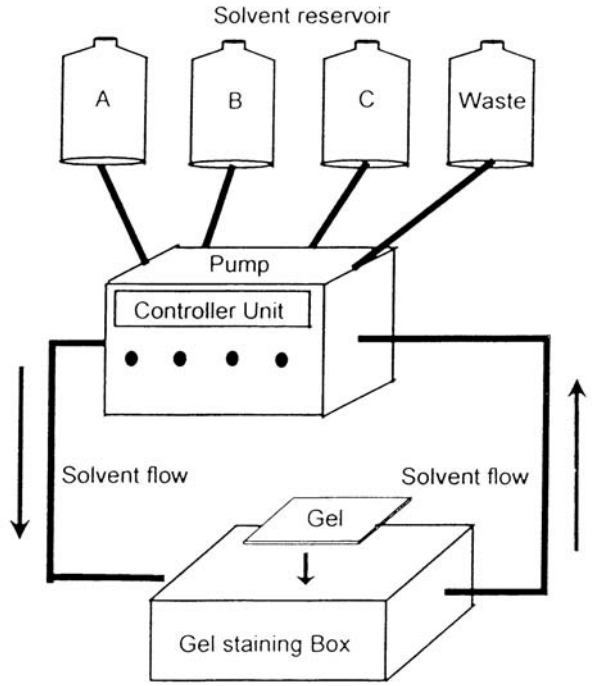
Filing a patent in Finland

HY/TKK

- alot of costs for the inventor
-alot hassle for the inventor
-no agreement with inventor
-great opportunity = this must be a joke!!

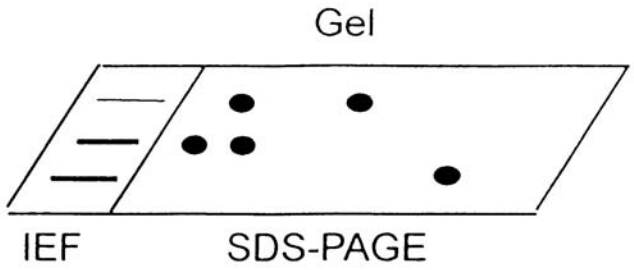
The Idea!

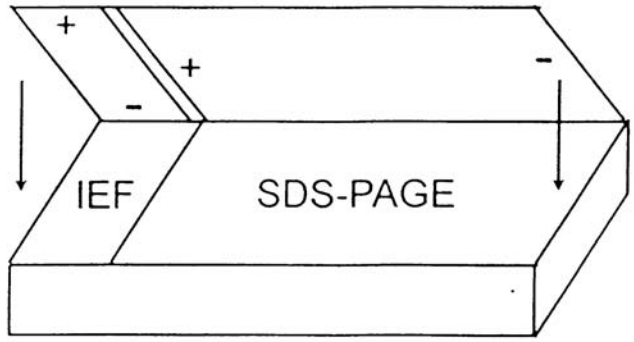
Automated stainer/destainer



Came out from GE-Healthcare

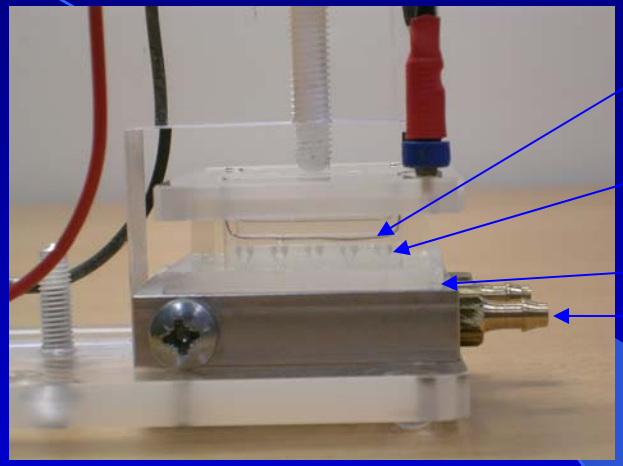
Automated 2-D

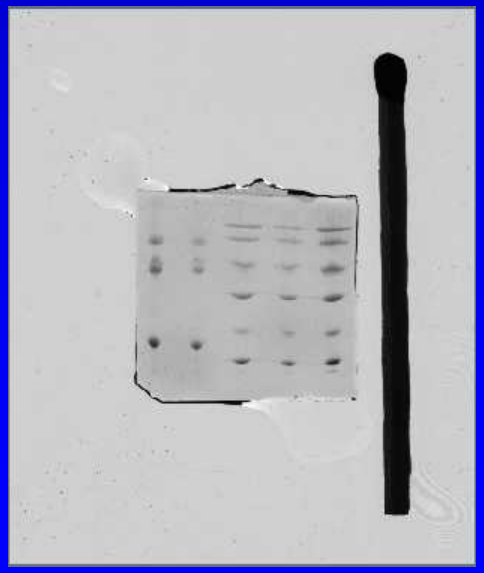


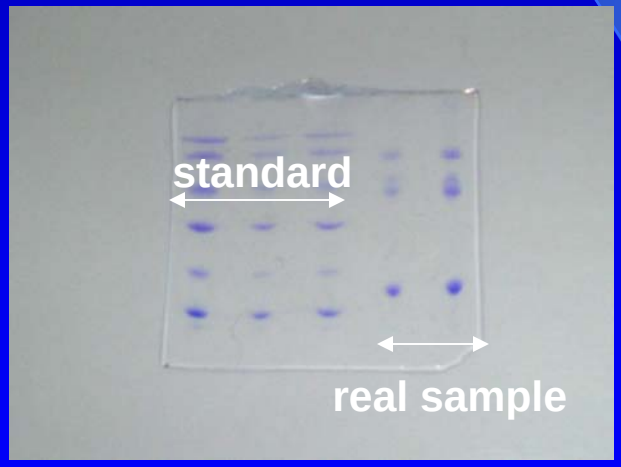


Protein Microchips for the Identification and quantification of Biomolecules

1-DE Chip

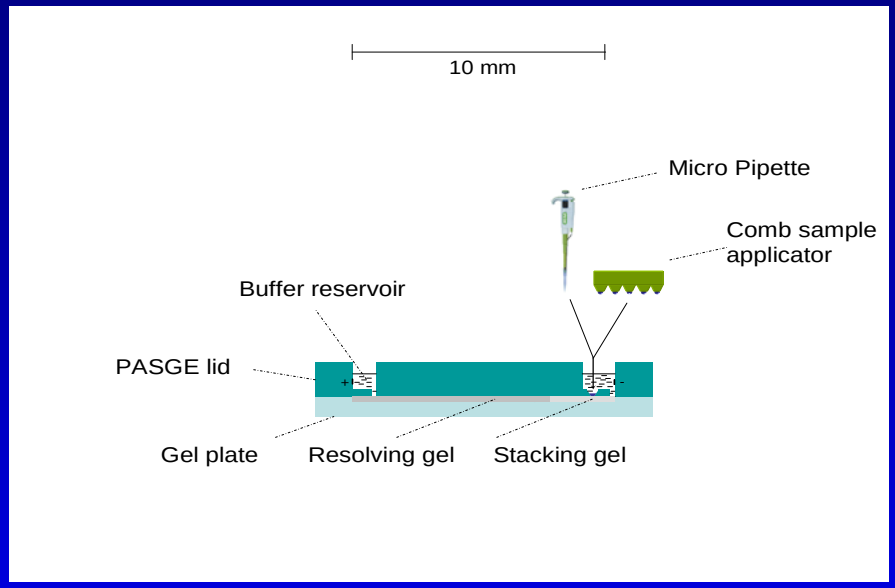


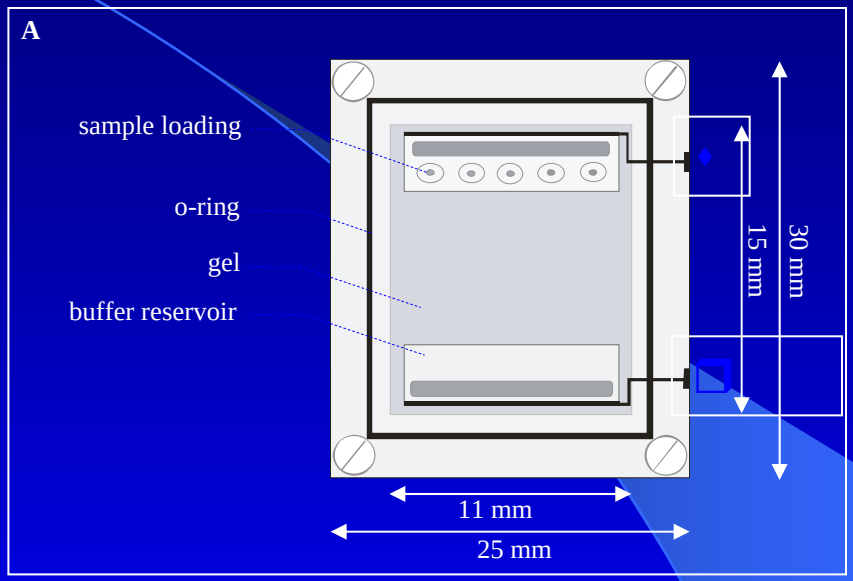


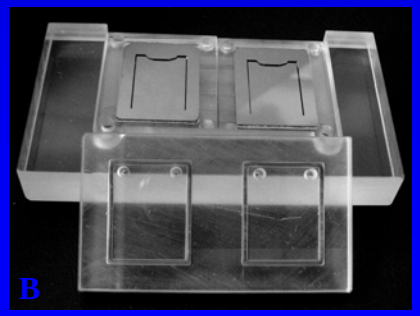


Running time 10 minutes

1-DE Chip


10 mm
Micro Pipette
Comb sample applicator
Buffer reservoir
PASGE lid
Gel plate
Resolving gel
Stacking gel


A
sample loading
o-ring
gel
buffer reservoir
15 mm
30 mm
11 mm
25 mm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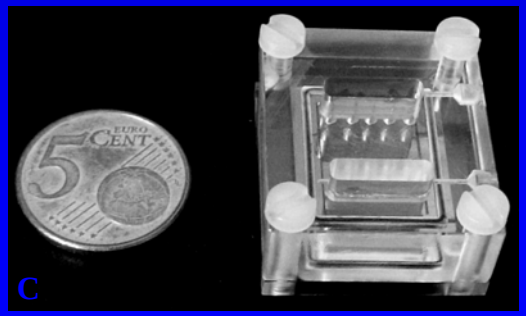
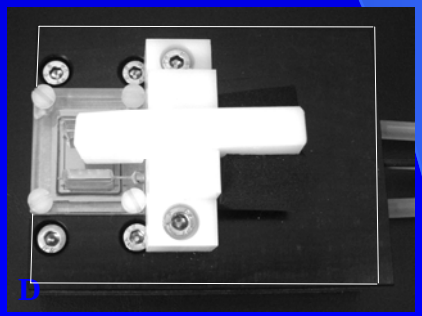

C


D

Turn to the Next PAGE

SDS-PAGE on protein minigels is such a routine analysis technique that it seems beyond question. Nevertheless, a new paper from Demianova et al. in *Molecular BioSystems* asks why we should be content with "mini" when "micro" can offer greater sensitivity and speed along with decreased sample usage. Although microfluidic devices for separating and visualizing proteins have been described, many are limited in the types of downstream analyses that are possible. Given the flexibility and popularity of SDS-PAGE, the authors stuck with this approach, but in a micro-gel format. Each gel has dimensions 15 × 75 × 0.75 mm, and is produced from about 68 µL of separating gel mixture and approximately 17 µL stacking gel solution. At this size, each lane can be loaded with 1.5 µL of sample, corresponding to a maximum of 1.5 µg of protein. Gels are run for approximately 10 min, a nine-fold decrease in separation time. The authors found that reproducibility is comparable to commercially prepared gels. Limit of detection was measured in comparison with a standard minigel, revealing a 10-fold advantage for the microscale device. Because SDS-PAGE is often a prelude to other analyses, showing the new gel system can be integrated with downstream procedures is essential if the approach is to win broad acceptance. Like standard minigels, the microscale SDS-PAGE gels can be used for Western blotting. Due to the reduced size, this leads to significant time savings during semi-dry blotting and in reduced antibody usage. The gels can also feed into peptide mass fingerprint analysis via mass spectrometry, although users should be aware that excision of the reduced-size protein bands can be technically challenging. As the device is fabricated from polymethyl methacrylate (with silicon dioxide-coated silicon for the gel chamber), it is cheap to produce. This property and its superior performance can be expected to convince many proteomics labs to take a step down from minigels to microgels.

Demianova et al. 2008. Development and application of a miniaturized gel electrophoresis device for protein analysis. Molecular BioSystems [Epub ahead of print, January 18, 2008].

Local Landmark

Like that of the ribosome, the structure of the spliceosome has been a high-priority research goal. Despite the recruitment of techniques from electron microscopy to single-particle reconstruction to the task, the resulting structures remain difficult to interpret. Some of the particular challenges presented by this macromolecular complex include its dynamic nature and the difficulty of purifying a sufficient number of particles at a usable concentration. Moreover, spliceosomal structural studies would ideally go beyond a global structure and allow the position of particular protein or RNA subunits to be pinpointed. Although gold immunolabeling can assist in this process, it is a method that entails substantial complexity and cost. In a Technical Report appearing in *Nature Structural and Molecular Biology*, Alcid and Jurica propose a new protein-based label for tagging RNA spliceosomal substrates. The strategy is a variation of previous studies that have used an MS2-MBP hybrid protein to tag RNA. This general approach uses the combination of an RNA-binding protein (MS2) with maltose-binding protein (MBP), which is useful in affinity purification schemes. Previously this strategy has been used for isolating spliceosomes prior to electron microscopy (EM). In their study, Alcid and Jurica put a new twist on both halves of the hybrid protein. For the RNA-binding protein, they used the coliphage coat protein PP7, and for its partner, they chose DnaN, the β subunit of prokaryotic Pol III. This latter factor, which they call simply "Beta," dimerizes to form a doughnut-shaped structure (which normally serves as a sliding clamp for the polymerase complex). Because the doughnut is large (with a 90-Å diameter) and has a highly recognizable shape, the authors hypothesized that it might act to broadcast its location. To exploit this system in order to point out the location of the 5′ or 3′ exon in the spliceosome, Alcid and Jurica created a pre-mRNA containing the PP7 target sequence either upstream of the splice donor or downstream of the splice acceptor. During spliceosome purification, an excess of Beta-PP7 hybrid protein was allowed to bind to the complexes, which were then purified and analyzed by EM images. By comparing averaged images in which the spliceosome was or was not labeled, a difference map showing the predicted location of the doughnut was produced. Aside from adding to the understanding of spliceosome structure, this paper establishes Beta-PP7 as a valuable label for EM analysis of RNA-containing macromolecular complexes.

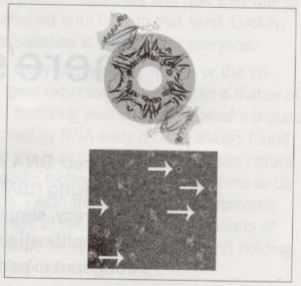
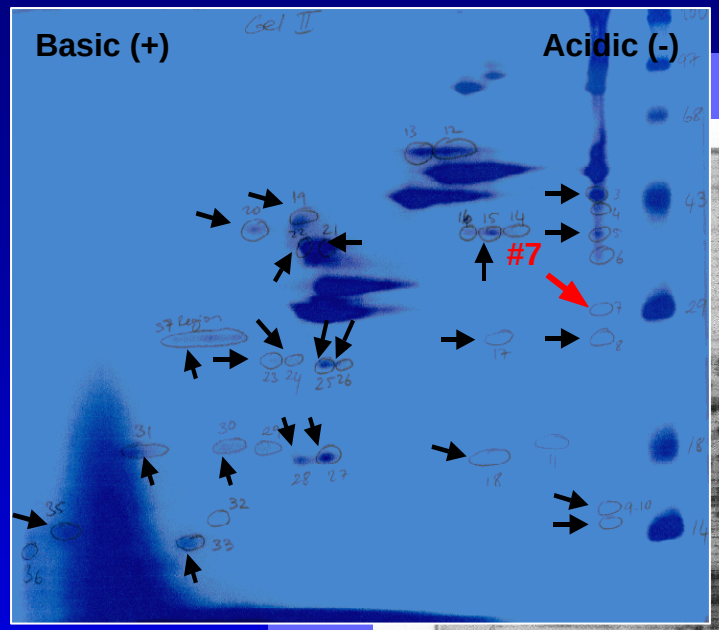


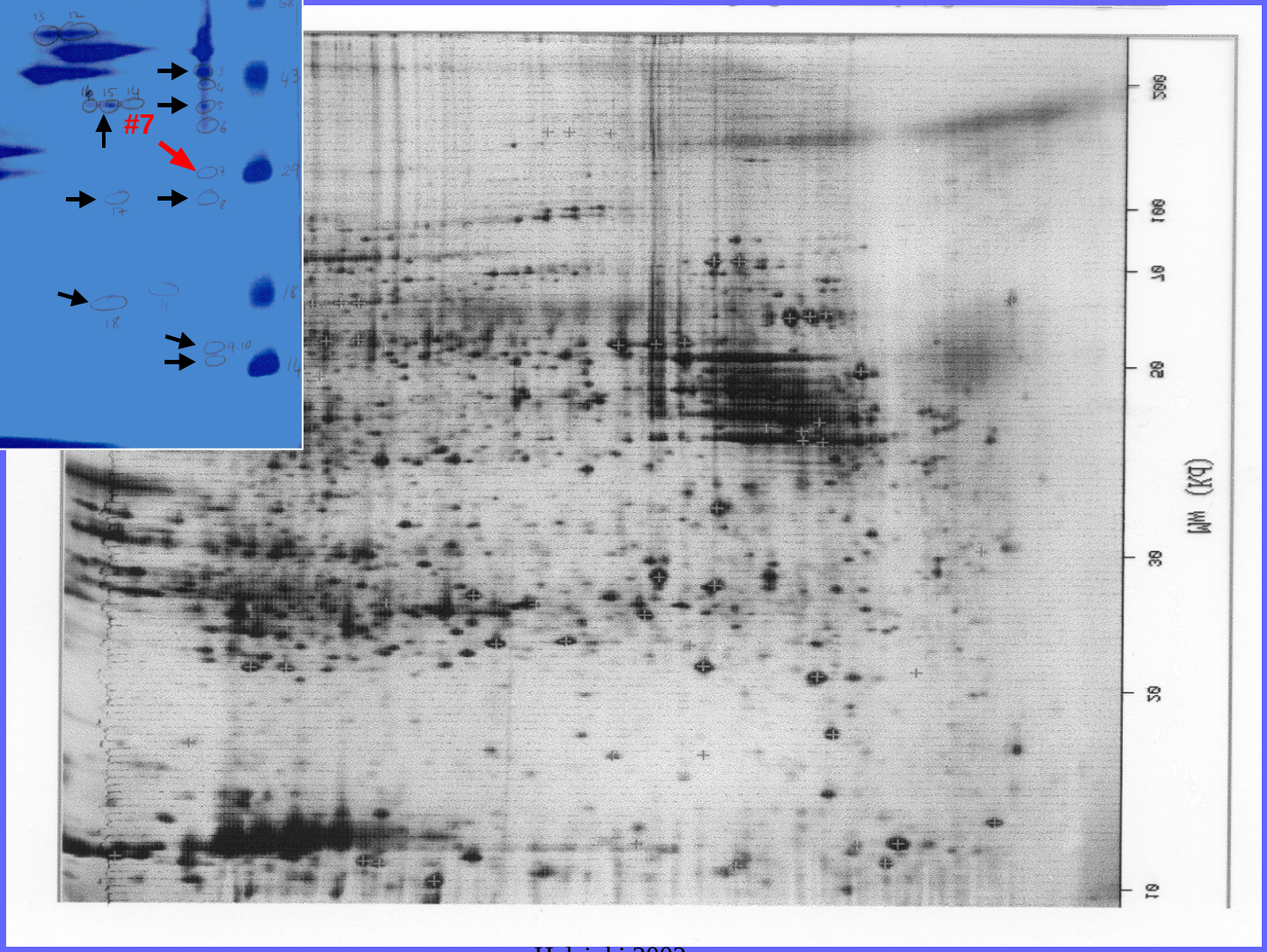
Image reprinted with permission. © 2008 Macmillan Publishers Ltd.

Alcid and Jurica. 2008. A protein-based EM label for RNA identifies the location of exons in spliceosomes. Nature Structural and Molecular Biology 15:213-215.

– Selected and written by **Nijsje Dorman**, a freelance writer in Boston, MA.

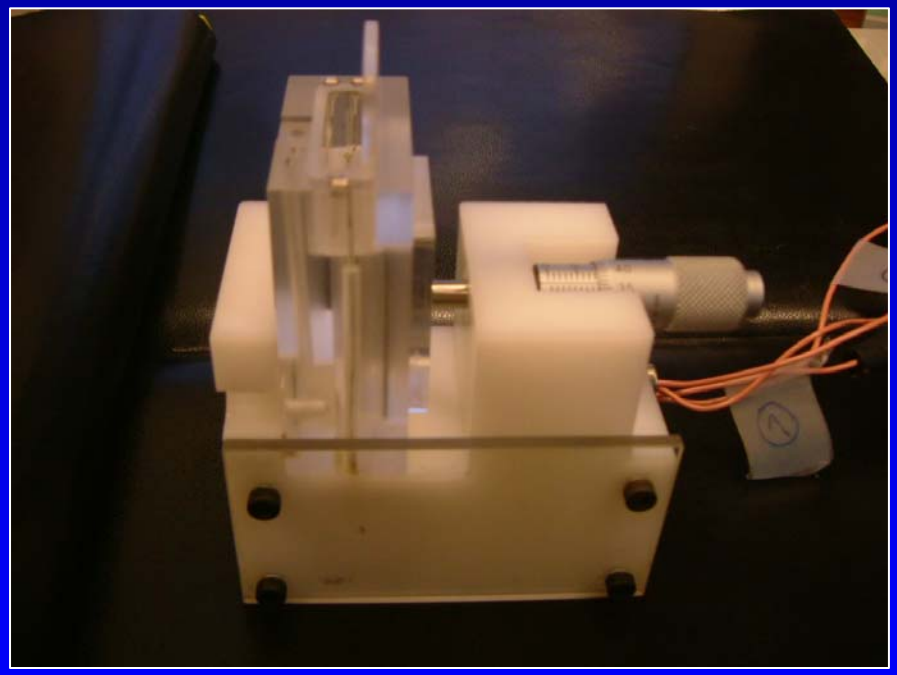
Proteomics performed by 2-dimensional Gel electrophoresis

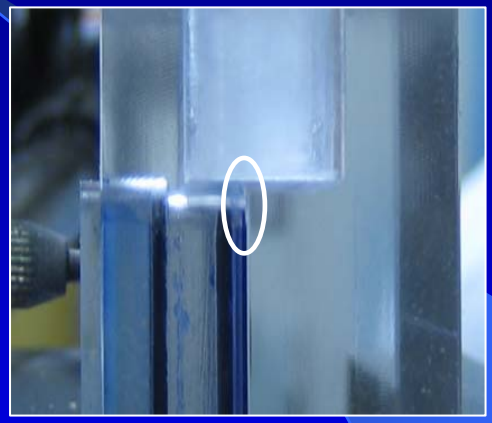


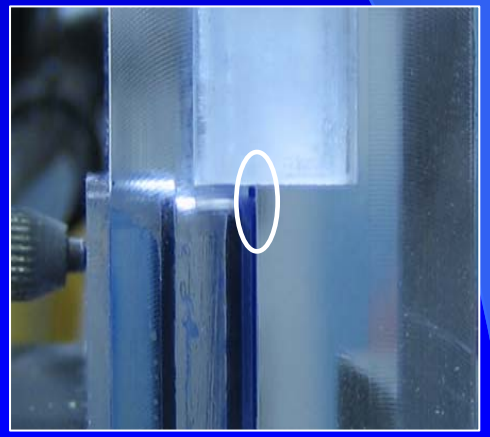


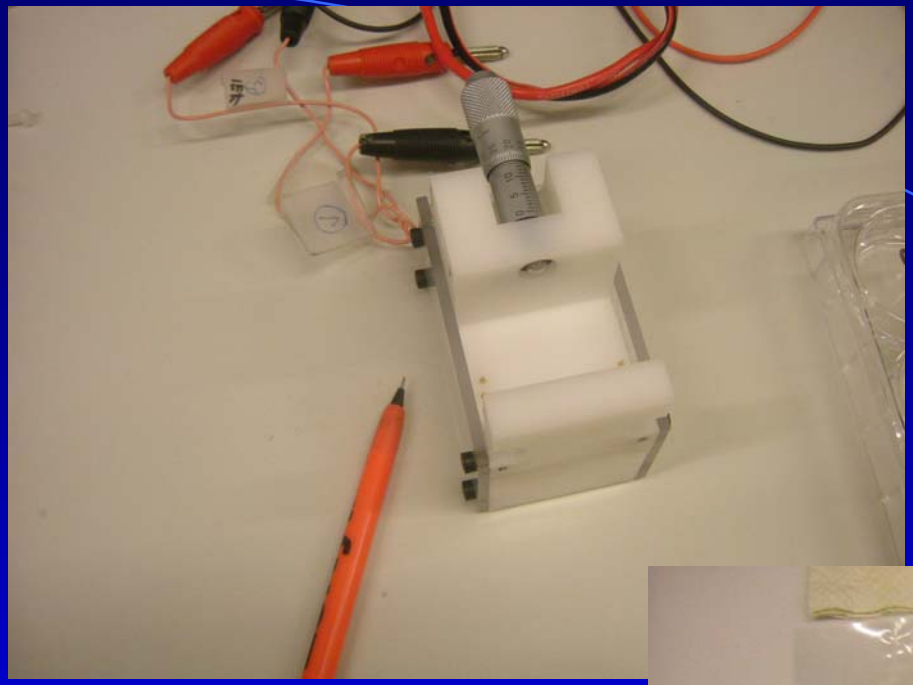
2-DE Chip

The compress system



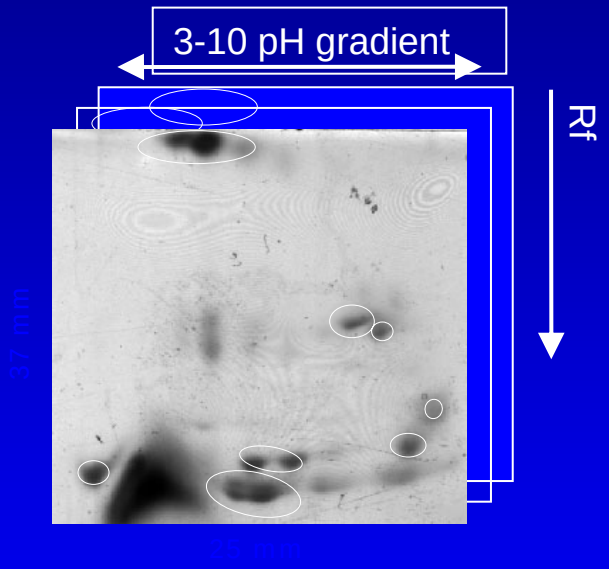






2-DE Chip

2-D map of IEF standards



Repeatability of 2-DE runs

Rf values (%)*		**pI position errors(%)***	
STDV	6,1	STDV	2,5
max	15	max	6
min	0,8	min	0,6

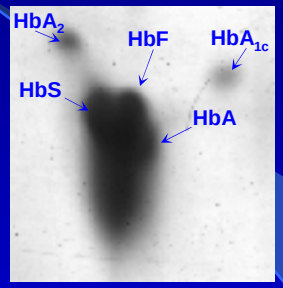
* comparison of 3 gels

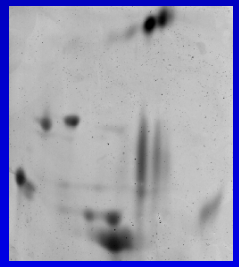
- 2-DE separation completed in **approx. 80 min**
- Limit of detection is **approx. 65 ng**

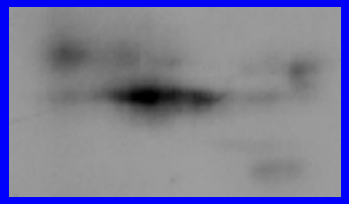
Running time 20-30 minutes

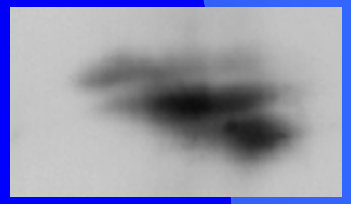
compress 2-DE system

- Performance
  - Native IEF and native PAGE
    - 5 variants of hemoglobin
    - pH 6.7 -7.7
  - Native IEF and SDS-PAGE
    - standard IEF proteins
    - pH 3-10
  - Denatured IEF and SDS-PAGE
    - GFAP protein variants expression differences
    - in control and Alzheimer diseased patients
    - pH 4-6



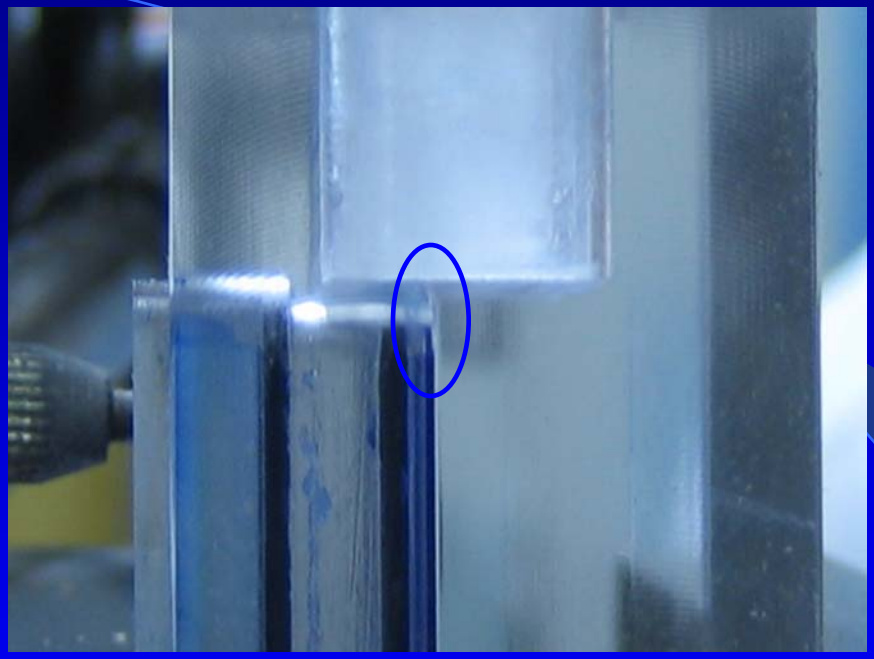




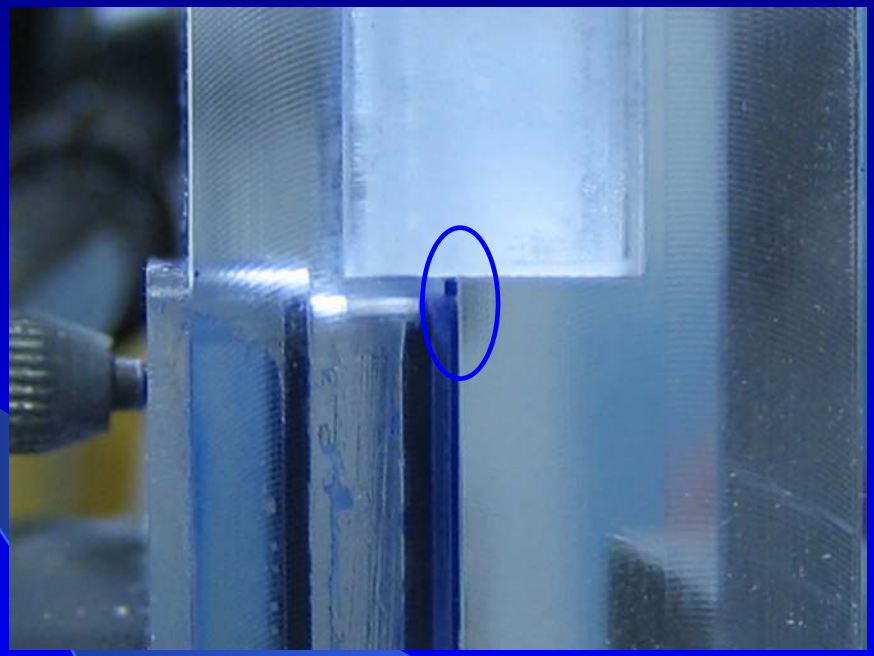


ComPres device/pressing of the gel

Before



After



Gel was been press 0,05 mm to obtained filling of the channel between IEF and PASGE gel

This is the only thing I have patented

Some details:

We patented first in England = entrance to EU

Then US, CAN, PTC-EU, AUS

All costs were covered by the inventors grants

All together

10.000€
for the first round

There was not much help of:

- Licentia
- UH/TKK

sp keep in mind that YOU have to do everything

What are your options?

You have several options:
1) grab some money from the investors…

…and you are lost

unless you find just one partner who is really interested in your idea and not in killing you

Let Licentia pay or get a loan…

…and you are lost

unless you keep track that Licentia really does the selling job!

Get a partner who can provide you with support and understanding…

…and you are saved

You might not get much money but you get support for several years

And you might get your invention to see the light!

Is that not what we scientists mostly hope for?