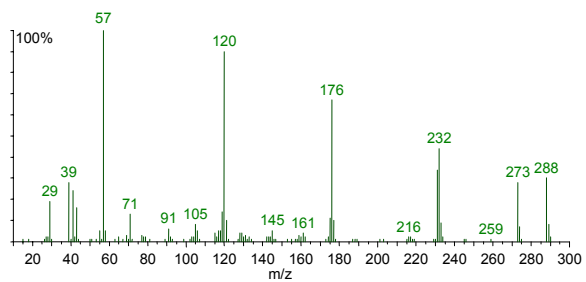
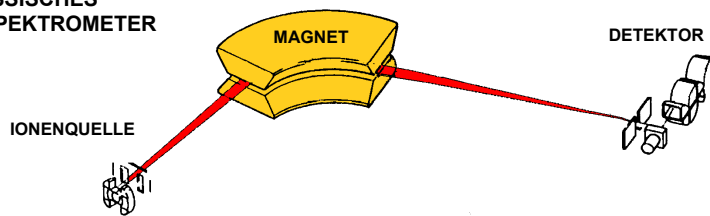




MASSENSPEKTROMETRIE

KLASSISCHES
MASSENSPEKTROMETER

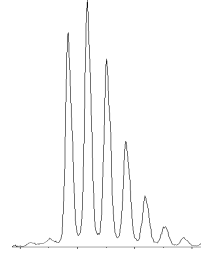


MASSENSPEKTROMETRIE: GESTERN - HEUTE - MORGEN

- 100 JAHRE MASSENSPEKTROMETRIE

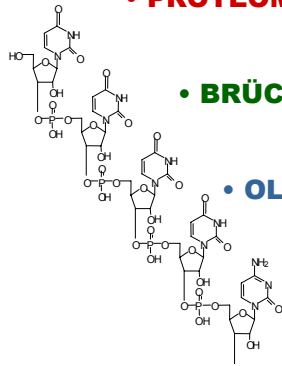
- ANWENDUNGEN IN DER BIOANALYTIK

- **PROTEOMICS**



- **BRÜCKENMUSTER VON SPINNENTOXINEN**

- **OLIGONUCLEOTID SEQUENZIERUNG**



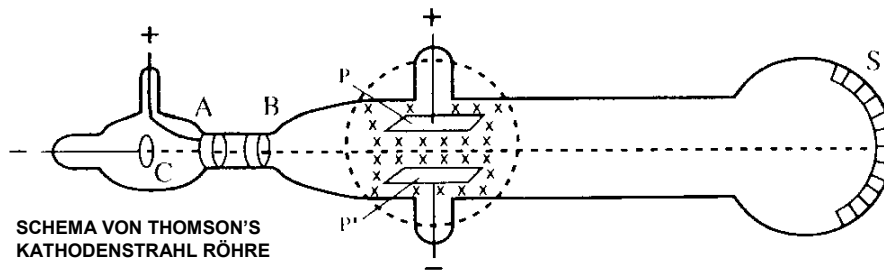
SIR JOSEPH JOHN THOMSON ENTDECKUNG DES ELEKTRONS (1897)



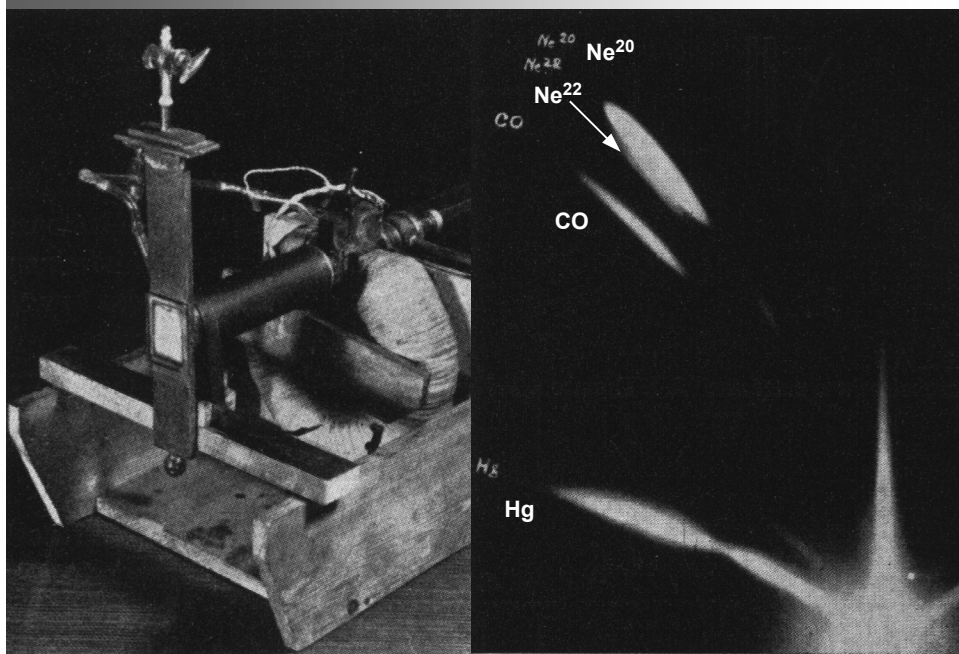
'AT FIRST THERE WERE VERY FEW WHO BELIEVED IN THE EXISTENCE OF THESE BODIES SMALLER THAN ATOMS. I WAS EVEN TOLD LONG AFTERWARDS BY A DISTINGUISHED PHYSICIST WHO HAD BEEN PRESENT AT MY 1897 LECTURE AT THE ROYAL INSTITUTION THAT HE THOUGHT I HAD BEEN PULLING THEIR LEGS.'

J.J. Thomson, *'Recollections and Reflections'*, G. Bell and Sons, London 1936.

⇒ NOBELPREIS FÜR PHYSIK 1908



THOMSON'S PARABEL-SPEKTROGRAPH (1910)

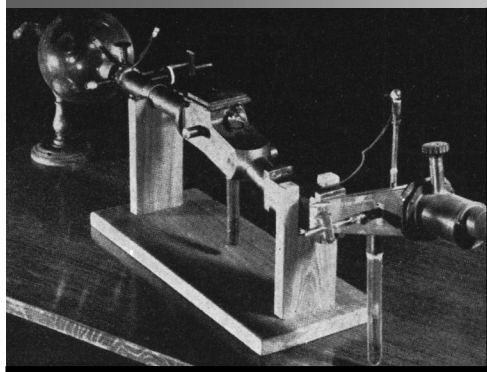


DIE 20ER JAHRE - DAS JAHRZEHT DER ISOTOPEN



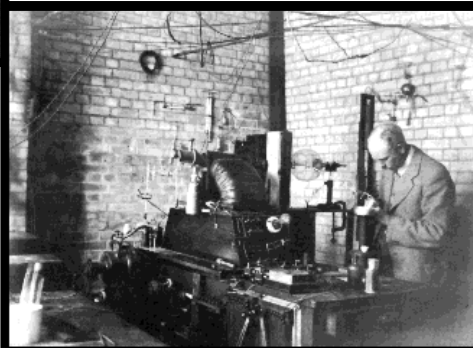
MASSENSPEKTROGRAPH VON F.W. ASTON (1919), SCIENCE MUSEUM LONDON

DIE 20ER JAHRE - DAS JAHRZEHT DER ISOTOPEN

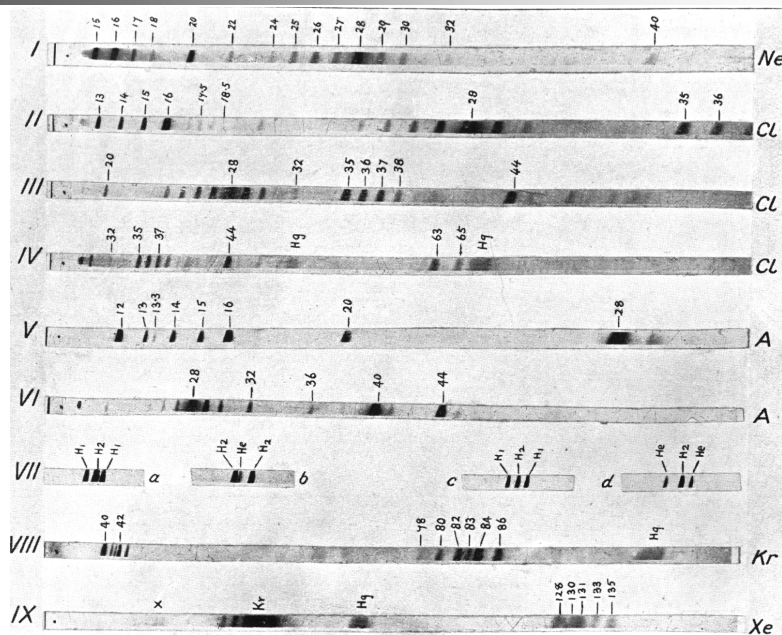


ASTON'S MASSENSPEKTROGRAPH
VORLÄUFER SPÄTERER
HOCHAUFLÖSENDER
MASSENSPEKTROMETER

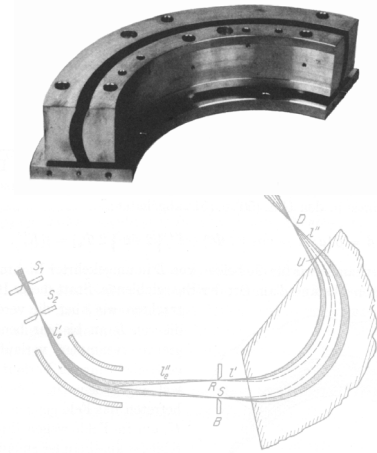
F.W. ASTON IM CAVENDISH
LABORATORY, CAMBRIDGE (1920)



ISOTOPEN SEPARATION (F.W. ASTON 1920)



DIE 30ER JAHRE - IONENOPTIKEN UND THEORIEN



**ERNEST LAWRENCE
ENTWICKELT DAS CYCLOTRON
(UC BERKELEY, 1931)**

$$\begin{aligned} & \psi \\ & - \text{tg} \\ & \text{tg} \psi = \frac{l'}{a+l'} \\ & \frac{l}{l'} \end{aligned}$$

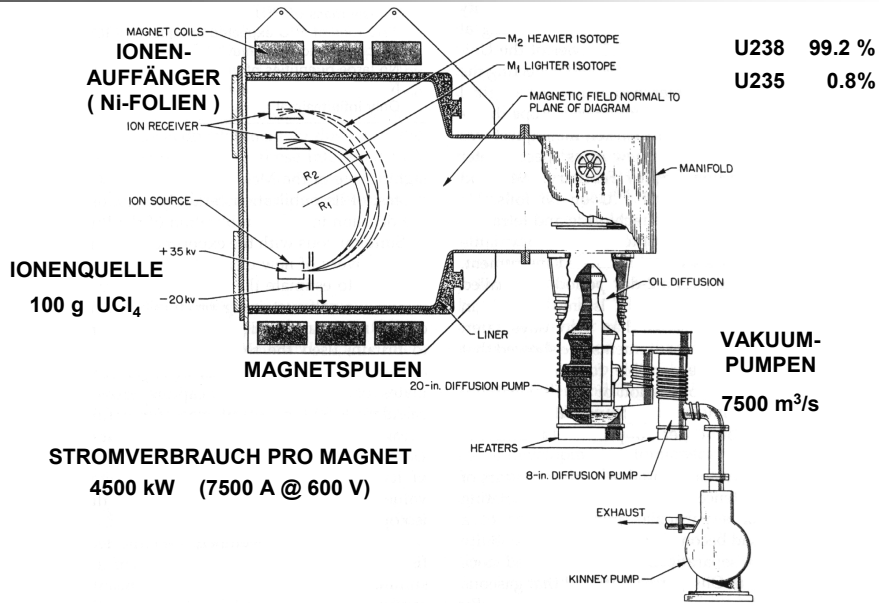
leitung der Linsenformel des magnetischen an errechnet die Bildweite l'' el [Gl. (9a)] unter Berücksic Gln. (10), (11), (12)

**HAROLD UREY ENTDECKT
DAS DEUTERIUM (1932)**

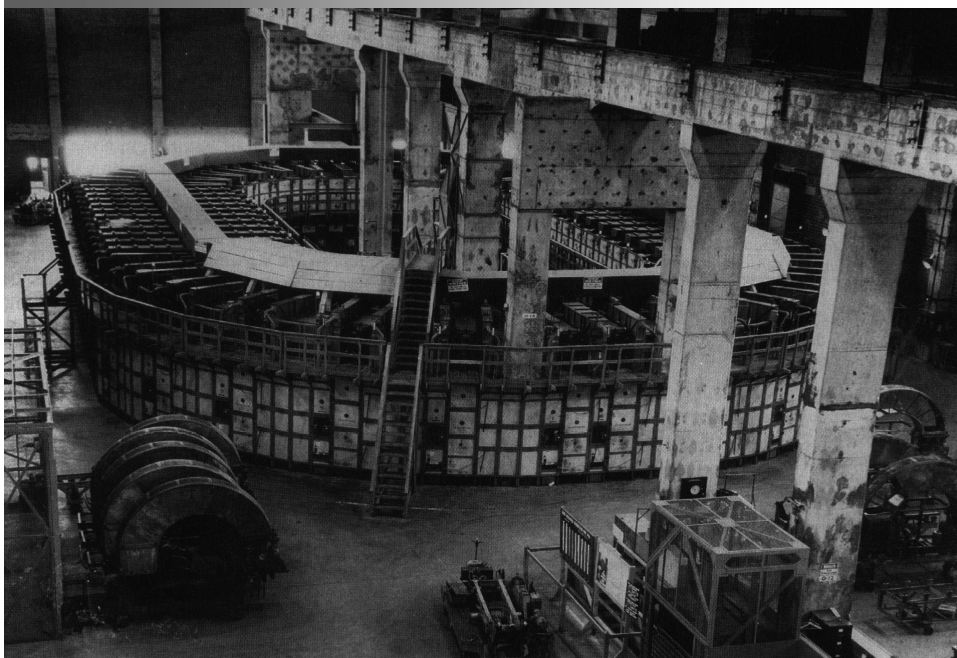
$$\begin{aligned} l'' &= \frac{a \cdot \text{tg} \chi}{1 - \text{tg} \chi \cdot \text{tg} \epsilon''} \quad 1 + \frac{\text{tg} \Phi + \text{tg} \psi \cdot \text{tg} \epsilon''}{1 - \text{tg} \Phi \cdot \text{tg} \psi} \\ &= -a \cdot \frac{\text{tg} \Phi + \text{tg} \psi}{1 - \text{tg} \Phi \cdot \text{tg} \psi + (\text{tg} \Phi + \text{tg} \psi) \cdot \text{tg} \epsilon''} \\ & \quad \frac{\text{tg} \Phi + \frac{l'}{a+l' \cdot \text{tg} \epsilon'}}{\text{tg} \Phi \cdot \frac{l'}{a+l' \cdot \text{tg} \epsilon'} + \left(\text{tg} \Phi + \frac{l'}{a+l' \cdot \text{tg} \epsilon'} \right) \cdot \text{tg} \epsilon'} \\ & \quad \frac{\text{tg} \Phi (a+l' \cdot \text{tg} \epsilon') + l'}{\Phi - a - l' \cdot \text{tg} \epsilon' - [\text{tg} \Phi (a+l' \cdot \text{tg} \epsilon') + l'] \cdot \text{tg} \epsilon'} \end{aligned}$$

**JOSEF MATTAUCH UND RICHARD HERZOG
ENTWICKELN DAS DOPELFOKUSSIERENDE
(HOCHAUFLÖSENDE) MASSENSPEKTROMETER
(WIEN 1934)**

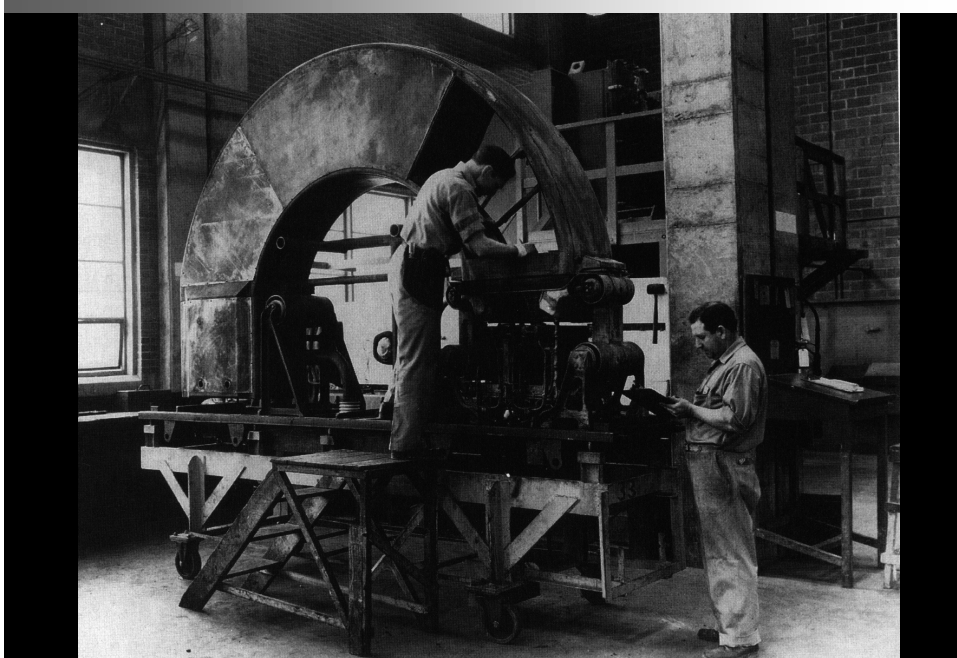
DER KRIEG - PRÄPARATIVE MASSENSPEKTROMETRIE DAS CALUTRON



PRÄPARATIVE MASSENSPEKTROMETRIE - DAS CALUTRON



PRÄPARATIVE MASSENSPEKTROMETRIE - DAS CALUTRON



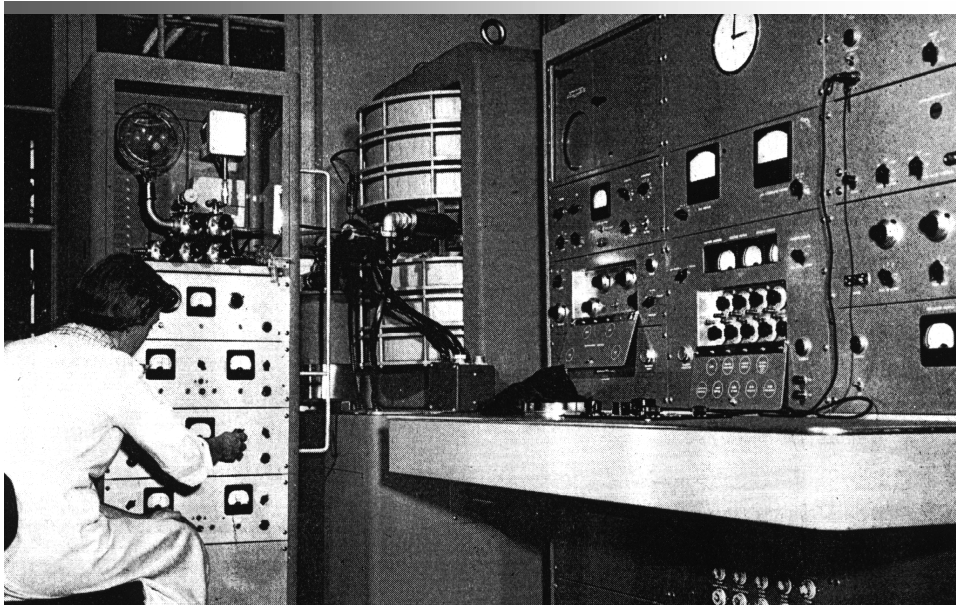
PRÄPARATIVE MASSENSPEKTROMETRIE - DAS CALUTRON



MAGNETSPULEN AUS REINEM SILBER VOR DER RÜCKGABE AN DAS US DEPARTMENT OF TREASURY (ca. 1948)

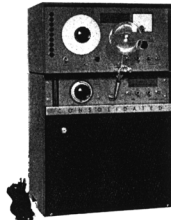
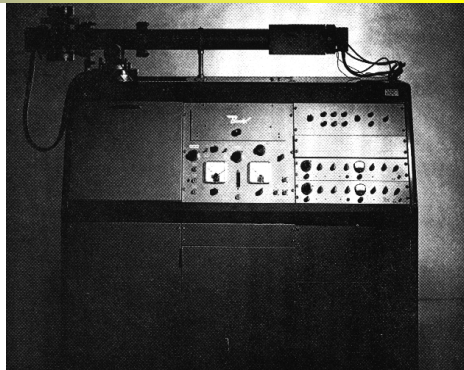
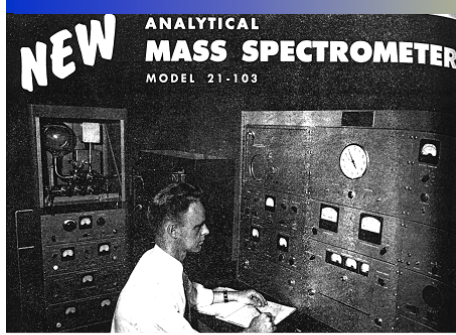
A TREASURY OFFICIAL WAS APPROACHED ABOUT THE POSSIBILITY OF LOANING SILVER TO A WARTIME EMERGENCY PROJECT. WHEN THE OFFICIAL ASKED ABOUT THE AMOUNT OF SILVER REQUIRED, HE WAS TOLD THAT THE PROJECT WOULD REQUIRE ABOUT 15'000 TONS OF THE METAL. HIS RESPONSE WAS 'SIR, WE MEASURE OUR SILVER IN OUNCES, NOT TONS'....

DIE 50ER JAHRE - KOMMERZIALISIERUNG



CEC Model 21-103 Sector Field Mass Spectrometer (1950)

DIE 50ER JAHRE - KOMMERZIALISIERUNG



**quick, accurate
gas analyses**

*with low-cost,
easy-to-operate,*

analytical mass spectrometer

available for batch or continuous analysis

This T.O.F.* analyzes anything

(almost)

There is something the Bendix® Time of Flight Mass Spectrometer won't analyze. Diamonds! But hand it any other material and you'll get your quantitative-qualitative analysis fast... and accurately. Its versatility is unsurpassed for analytical purposes, research projects or industrial process control.

Depending on project needs and equipment, you can get up to 100,000 spectra per second, unit resolution up to mass 350 and a sensitivity of 1 to 5 ppm. With the analog

output system you can record both positive and negative ion spectra and can simultaneously record up to six preselected masses.

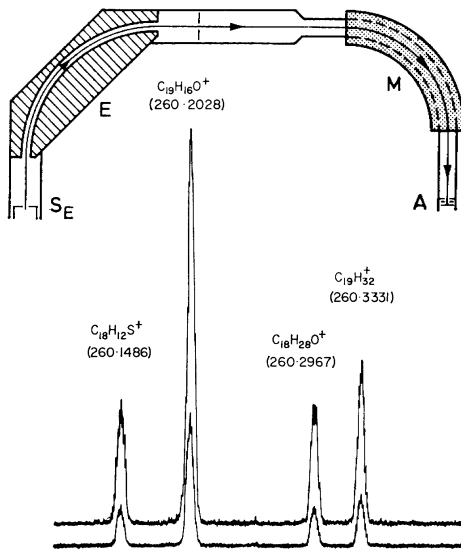
The unit is compact and easy to move. Maintenance involves little more than knocking the dust off once a week. And the list of things it can do in the way of analyzing won't even give the dust a chance to collect. Models range from \$17,000 to \$100,000. What would you like to analyze? Dept. A-3, 3625 Hauck Road, Cincinnati 41, Ohio.

*Time of Flight Mass Spectrometer

Cincinnati Division

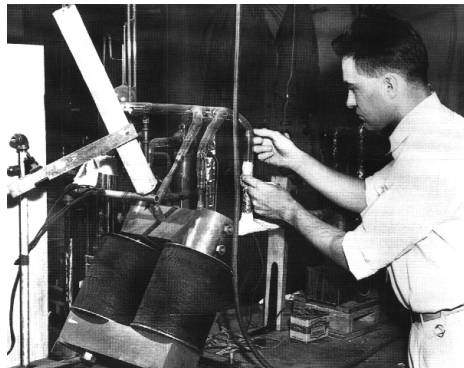


DIE 50ER JAHRE - HOCHAUFLÖSENDE MASSENSPEKTROMETRIE

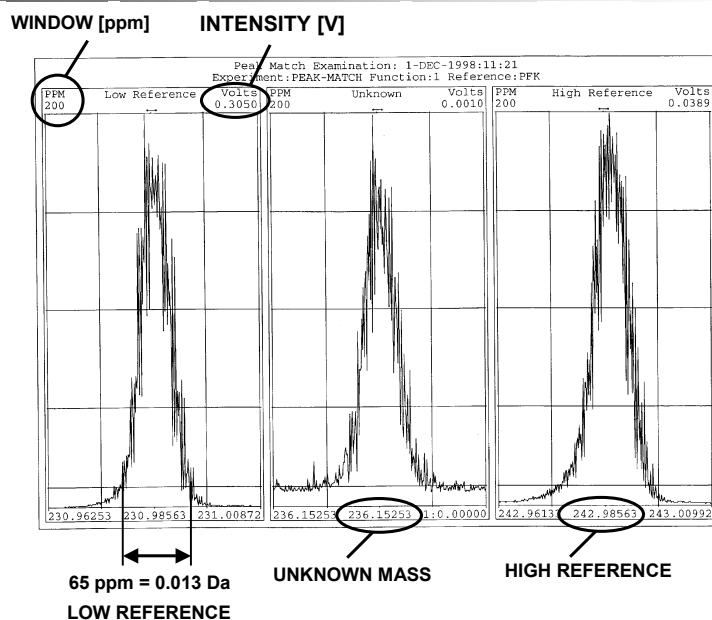


**MOLECULES HAVING THE SAME MASS
NUMBERS BUT DIFFERING IN WEIGHT BY
AN AMOUNT DETERMINED ONLY BY THE
DIFFERENCE IN BINDING ENERGIES OF
THE NUCLEAR PARTICLES CAN BE
CLEARLY RESOLVED...**

ALFRED O. NIER, SCIENCE 121, 1955, 740.



ACCURATE MASS DETERMINATION (PEAK MATCHING)



ACCURATE MASS DETERMINATION (PEAK MATCHING)

THEORETICAL MASS

Elemental Composition

Date : 1-DEC-1998

Heteroatom Max: 10 Ion: Both Even and Odd

Limits:

236.152530 5.0 -0.5 0 0 0 0 0 0 0 0

20.0 30 30 10 10 5 10 5 5 5

Mass	mDa	PEM	Calc. Mass	DBE	C	H	N	O	F	Si	P	Cl	Br
236.152530	0.0	0.1	236.152546	0.0	11	26			1	1	1		
	-0.1												
	-0.3	-1.1	236.152278	1.5	8	19	5	2	1				
	0.3	1.1	236.152791	0.5	9	23	3	2			1		
	0.4	1.7	236.152936	1.0	5	20	8	1		1			
	0.4	1.8	236.152965	0.5	10	23	3	1				1	
	-0.5	-2.1	236.152034	1.0	10	22	2		2	1			
	-0.9	-3.8	236.151623	1.0	8	21	6						1
	-1.1	-4.6	236.151448	1.0	7	21	6	1			1		
	1.1	4.6	236.153621	1.0	10	21	2	3	1				

EXPERIMENTAL MASS

DEVIATION FROM THEORETICAL MASS

ELEMENTAL COMPOSITION

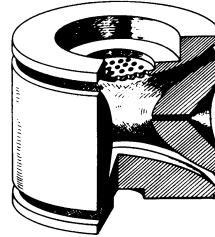
ERROR OF ACCURATE MASS DETERMINATION ON MICROMASS AUTOSPEC: ± 2 ppm

DIE 50ER JAHRE - QUADRUPOLE UND IONENSPEICHER

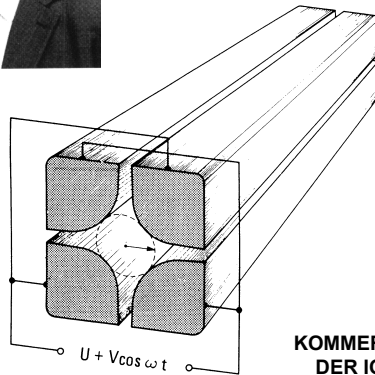


WOLFGANG PAUL BESCHREIBT
DAS ELEKTRISCHE MASSENFILTER
(QUADRUPOLE ANALYSATOR)

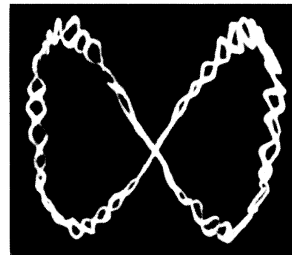
(W. Paul, H. Steinwedel,
Z. Naturforsch. 8a, 1953, 448.)



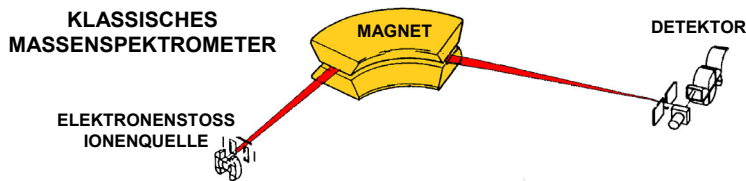
PRINZIP DES IONENSPEICHERS
1958 ERSTMALS BESCHRIEBEN
(W. Paul)



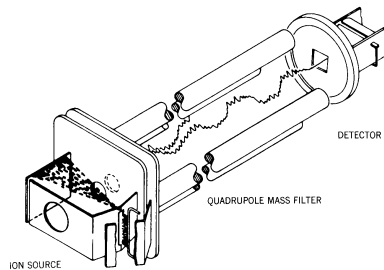
KOMMERZIALISIERUNG
DER ION TRAP 1984
(George Stafford,
Finnigan Corporation)



DIE 60ER JAHRE - QUADRUPOLE-MS, GC/MS KOPPLUNG, TANDEM MASSENSPEKTROMETRIE



GASPHASEN-VERHALTEN
ORGANISCHER VERBINDUNGEN



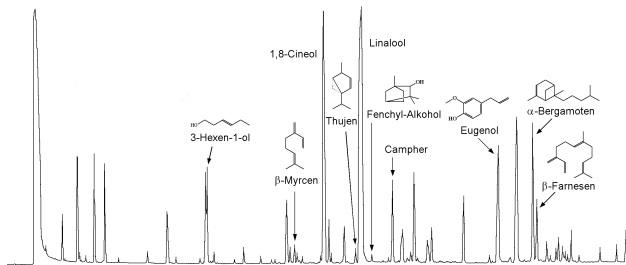
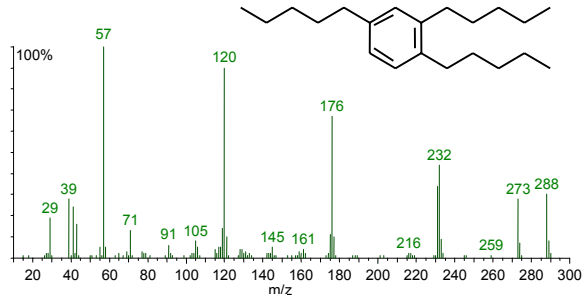
ERSTES KOMMERZIELLES
GC-QUADRUPOLE-MS
(FINNIGAN 1968)



TANDEM-MASSENSPEKTROMETRIE
(McLafferty, Jennings 1967)

DIE 70ER JAHRE - KLASSISCHE ORGANISCHE MASSENSPEKTROMETRIE

**STRUKTURAUFKLÄRUNG
ORGANISCHER VERBINDUNGEN
EI-MS & EI-MS/MS**



**GC/MS ZUR
NATURSTOFF-ANALYSE**

DIE 70ER JAHRE - EXTRATERRESTRICHE MASSENSPEKTROMETRIE

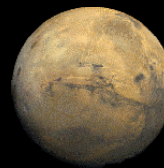


**1969-1972: SECHS MISSIONEN
ZUM MOND MIT GC/MS
KEINE BEWEISE FÜR LEBEN**

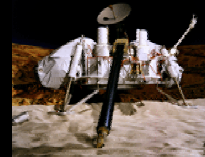
**MINIATURISIERTE MASSENSPEKTROMETER AN
BORD VON SATELLITEN ZUR UNTERSUCHUNG
DER ÄUSSEREN ERDATMOSPHERE (SEIT 1961)**



**PIONEER 13
MISSION ZUR VENUS
MIT GC/MS (NASA 1979)**



**VIKING MISSION ZUM MARS:
VIKING LANDER MIT GC/MS
ZUR UNTERSUCHUNG DER
MARS-ATMOSPHERE
(NASA 1975)**



DIE 80ER JAHRE - GRUNDSTEINE HEUTIGER BIOANALYTIK

SANFTE IONISIERUNGSMETHODEN

FAST ATOM BOMBARDMENT (BARBER 1981)

MALDI (TANAKA 1988, KARAS & HILLENKAMP 1988)

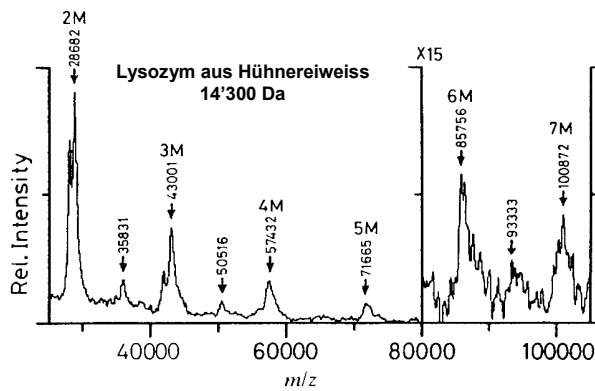
ELECTROSPRAY (DOLE 1984, FENN 1988)

Protein and Polymer Analyses up to m/z 100 000 by Laser Ionization Time-of-flight Mass Spectrometry

Koichi Tanaka¹, Hiroaki Waki, Yutaka Ido, Satoshi Akita, Yoshikazu Yoshida
and Tamio Yoshida
Shimadzu Corporation, Nishimokyo-Kuwaracho, Nakagyo-ku, Kyoto 604, Japan



Koichi Tanaka

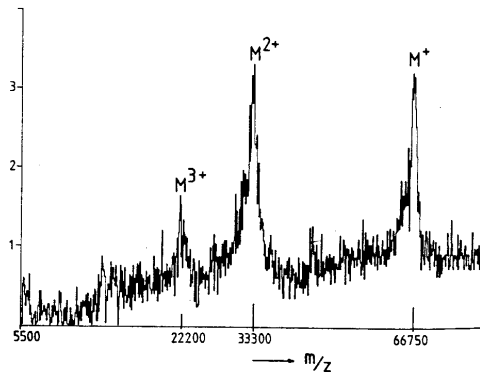


Rapid Commun. Mass Spectrom. 2, 1988, 151-153.

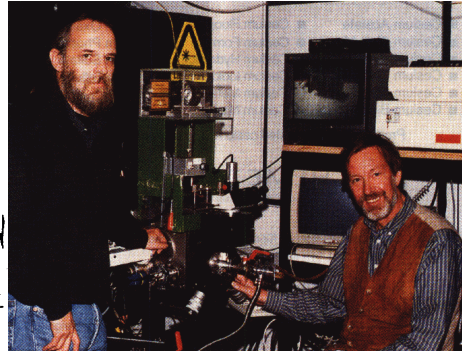
CORRESPONDENCE

Laser Desorption Ionization of Proteins with Molecular Masses Exceeding 10 000 Daltons

M. Karas and F. Hillenkamp,
Anal. Chem. 60, 1988, 2299-2301.



Serum Albumin aus Rinderblut
66'600 Da



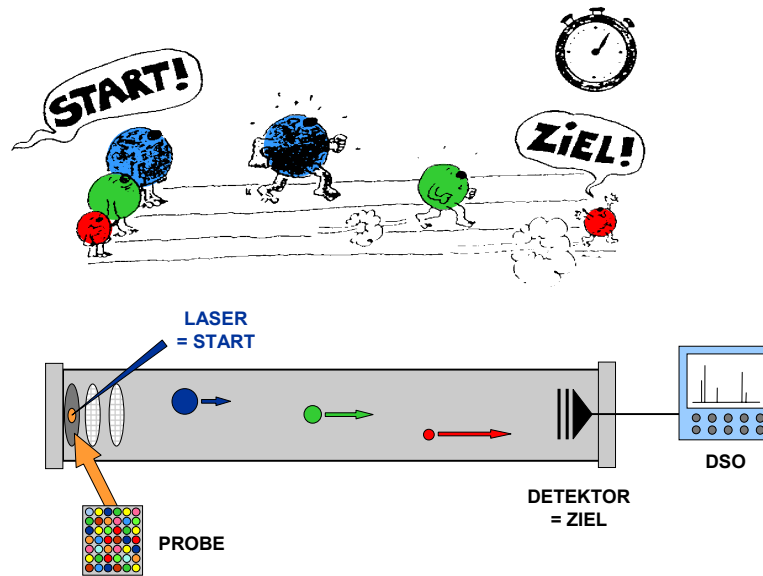
M. Karas und F. Hillenkamp

MATRIX-ASSISTED LASER DESORPTION/IONIZATION (MALDI)

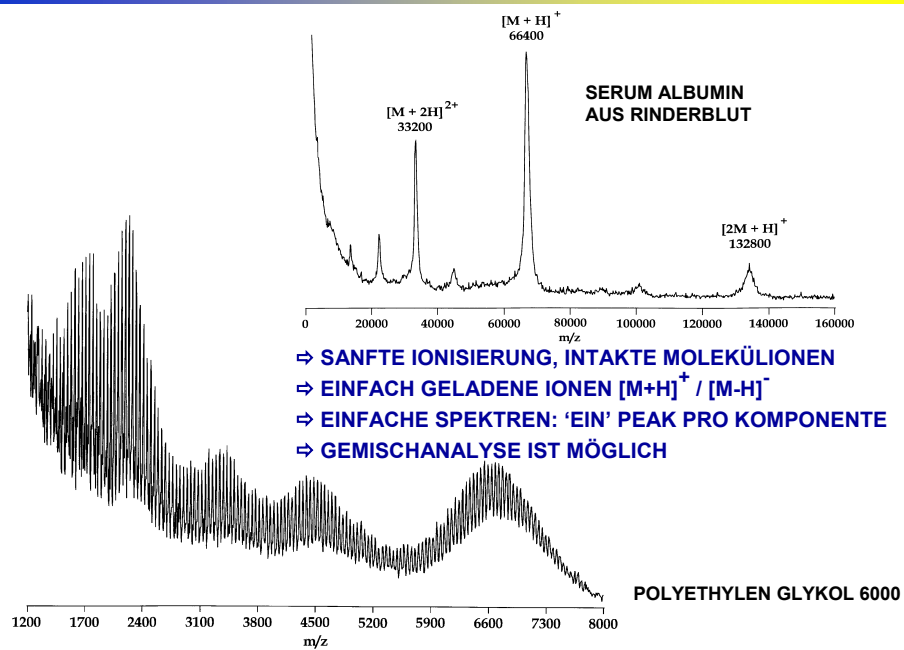
2,5-Dihydroxy-benzoesäure und Cytochrom c

The diagram illustrates the MALDI process. An "Energiericher Primärstrahl UV-LASER 337 nm, 3 ns" (energetic primary laser beam) strikes a surface of "MATRIX-MOLEKÜLE" (matrix molecules). This creates a "Kollisionskette" (collision chain) that leads to the desorption of particles. The desorbed particles include "Intaktes, protoniertes Biomolekül" (intact, protonated biomolecule) represented as a red circle with "[M+H]⁺", and "Desorbierte Partikel Ionen, Neutralteilchen, Elektronen" (desorbed particles: ions, neutral particles, electrons) represented as smaller orange circles with various symbols. Two SEM images, (a) and (b), show protein crystals. Image (a) is labeled "100 Shots @ 3.1 μJ" and image (b) is labeled "350 Shots @ 3.1 μJ". Both images include a 10 μm scale bar.

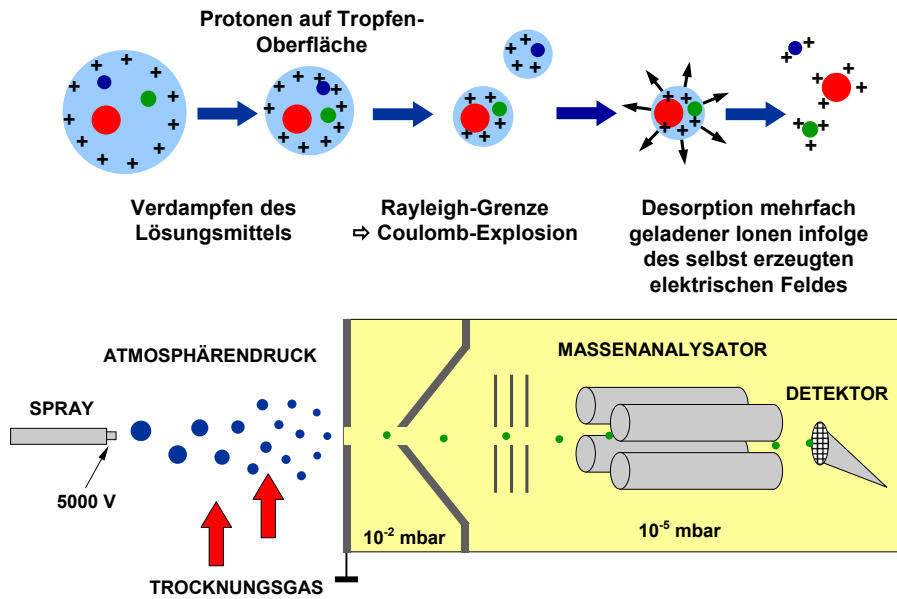
MALDI-TIME-OF-FLIGHT MASSENSPEKTROMETRIE



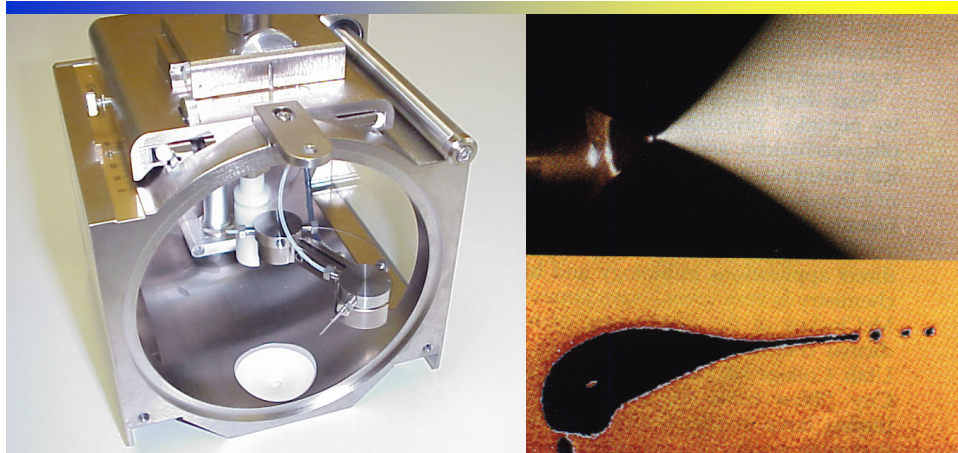
MALDI-TIME-OF-FLIGHT MASSENSPEKTROMETRIE



ELECTROSPRAY IONISIERUNG



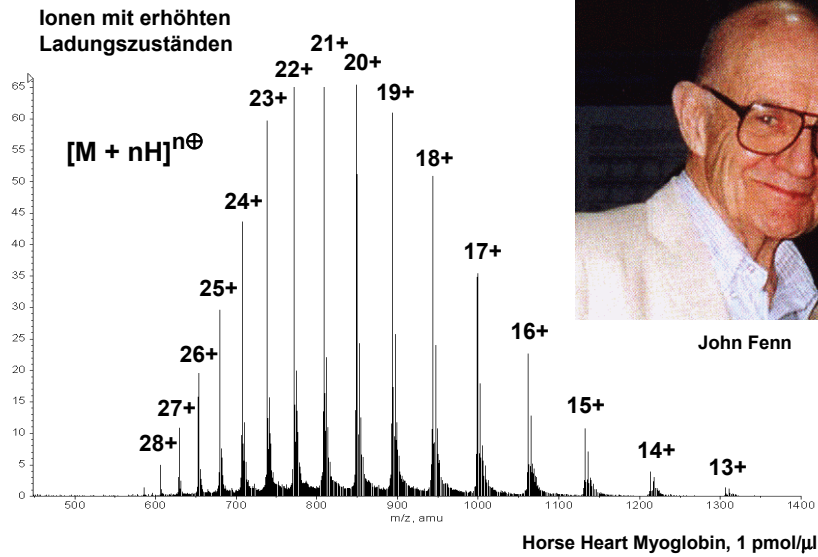
ELECTROSPRAY IONISIERUNG



- ⇒ SANFTE IONISIERUNG
- ⇒ MEHRFACH GELADENE IONEN
- ⇒ IONISIERUNG DIREKT AUS LÖSUNG
- ⇒ LC/MS KOPPLUNG
(GEMISCHTRENNUNG, REINIGUNG)

FLUSSRATEN 2 - 2000 $\mu\text{l}/\text{min}$
 PROBENVOLUMEN > 2 μl
 KONZENTRATION > 100 fmol/ μl

ELECTROSPRAY IONISIERUNG



John Fenn

MASSENSPEKTROMETRIE HEUTE

ORGANISCHE MS

NIEDERMOLEKULARE ORGANIKA
 STRUKTURAUFKLÄRUNG,
 IDENTIFIZIERUNG, QUANTIFIZIERUNG
 SYNTHESE, NATURSTOFFCHEMIE,
 UMWELTANALYTIK, FOOD,
 TOXIKOLOGIE, KRIMINALISTIK,
 ARCHÄOLOGIE
 EI-MS, FAB, ESI-MS
 GC/MS, LC/MS, MS/MS

MS IN DER BIOANALYTIK

BIOMOLEKÜLE GROSSER MASSER
 LABILE VERBINDUNGEN
 MASSENBESTIMMUNG, SEQUENZEN,
 MODIFIKATIONEN, IDENTIFIZIERUNGEN
 BIO-ORGANISCHE CHEMIE,
 BIOCHEMIE, BIOLOGIE, MEDIZIN
 ESI-MS, MALDI-MS
 LC/MS, MS/MS

ANORGANISCHE MS

METALLIONEN (ICP-MS)
 FESTKÖRPER-OBERFLÄCHEN (SIMS)
 GASANALYTIK (EI-MS & GC/MS)

DIE 90ER JAHRE - AUTOMATISIERUNG, HIGH-THROUGHPUT UND PROTEOMICS



GENOMICS:

- DNA SEQUENZ-ANALYSE
- STATISCHE INFORMATION
- NUR CODIERTE SEQUENZINFORMATION
- VIELE OPEN READING FRAMES

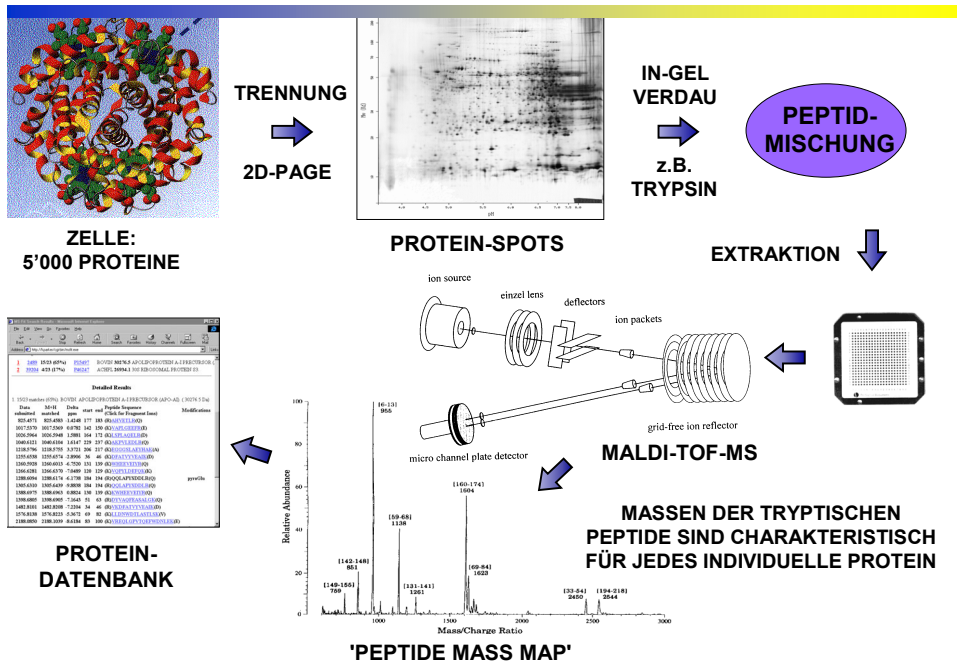
PROTEOMICS:

- UMFASSENDE PROTEIN ANALYSE
- ABBILD DER ZELLE ZU BESTIMMTEM ZEITPUNKT
- ERFASSEN DES EXPRESSIONSMUSTERS
- DYNAMIK, UP/DOWN REGULIERUNG
- ERFASSEN VON MODIFIKATIONEN (PTMs)
- MEHR ALS 1 PROTEIN PRO DNA-SEQUENZ
- PROTEIN-PROTEIN WECHSELWIRKUNGEN

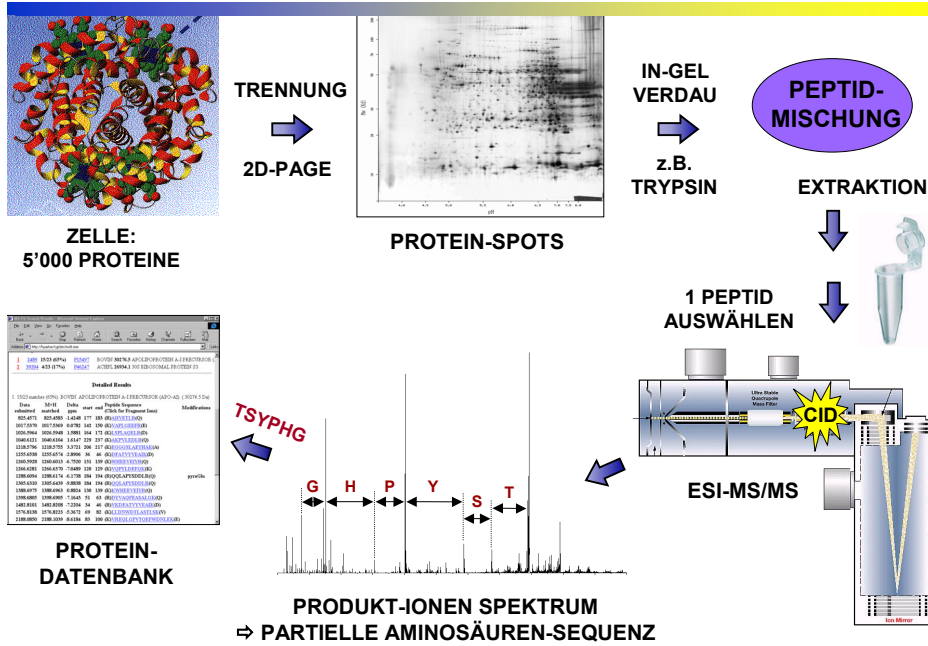
PROTEOM:

- TOTALER PROTEINGEHALT EINER ZELLE
(M. Wilkins, 1995)

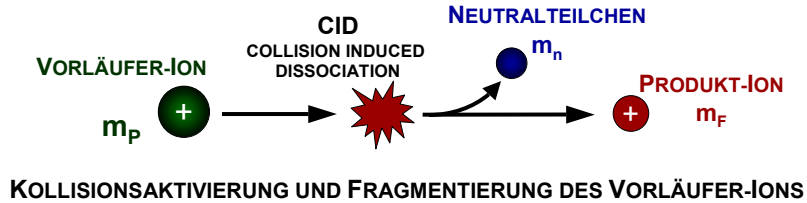
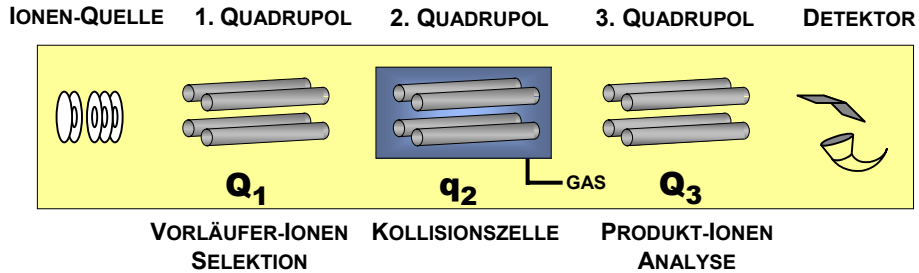
PROTEIN IDENTIFIZIERUNG MIT PEPTIDE MASS MAPPING



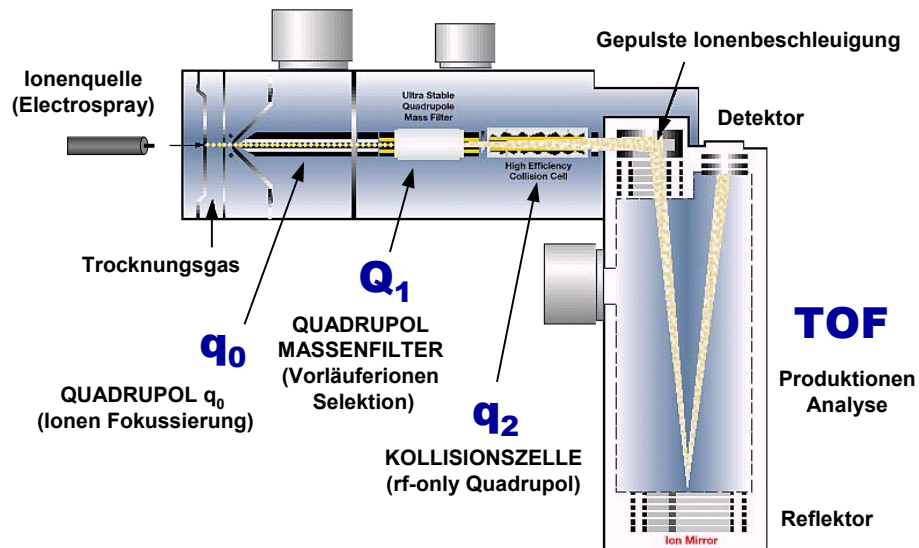
PROTEIN IDENTIFIZIERUNG MIT MS/MS



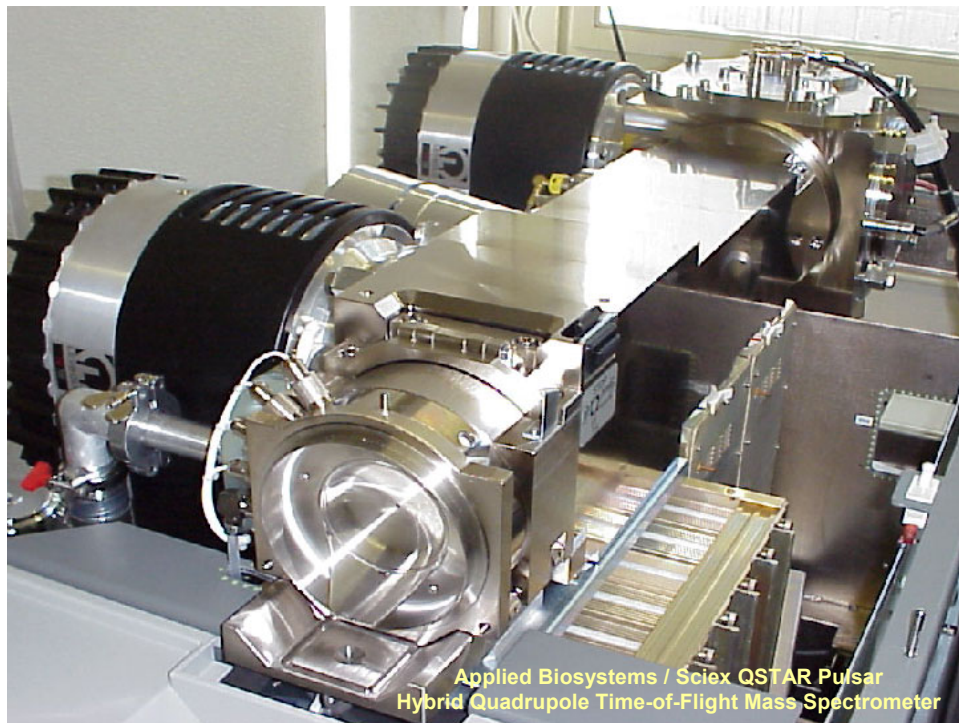
TANDEM-MASSENSPEKTROMETRIE MIT DEM TRIPLE-QUAD



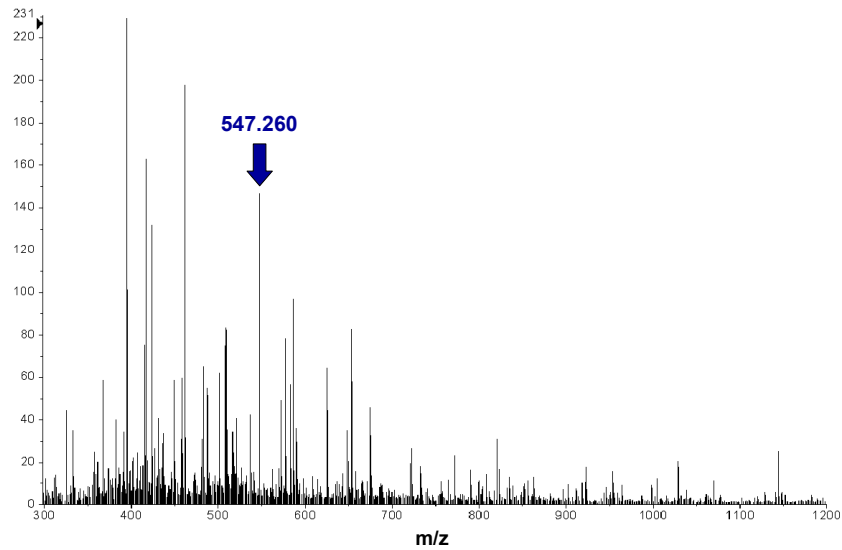
MODERNE TANDEM-MASSENSPEKTROMETER: QqTOF



Applied Biosystems / Sciex QSTAR Pulsar Hybrid Quadrupole Time-of-Flight Mass Spectrometer

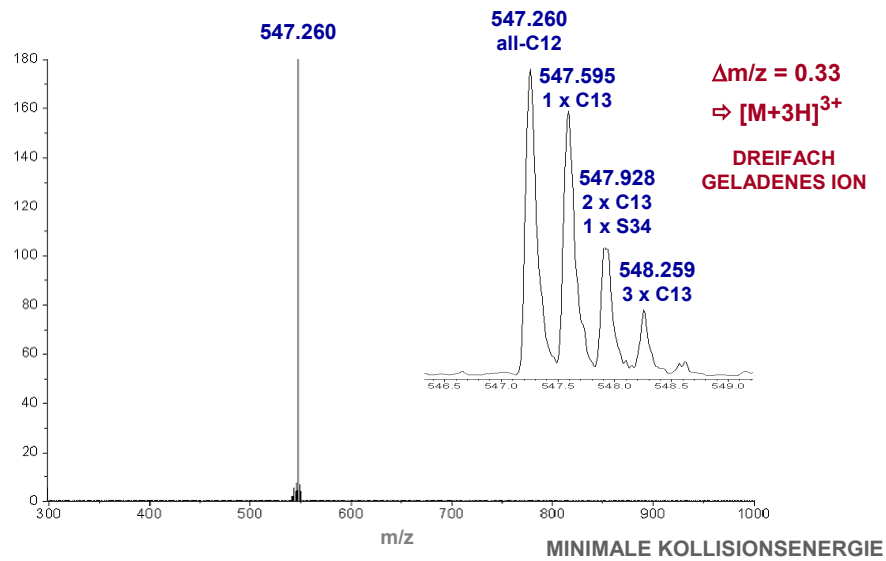


ESI-MS EINES TRYPTISCHEN PEPTID-GEMISCHES

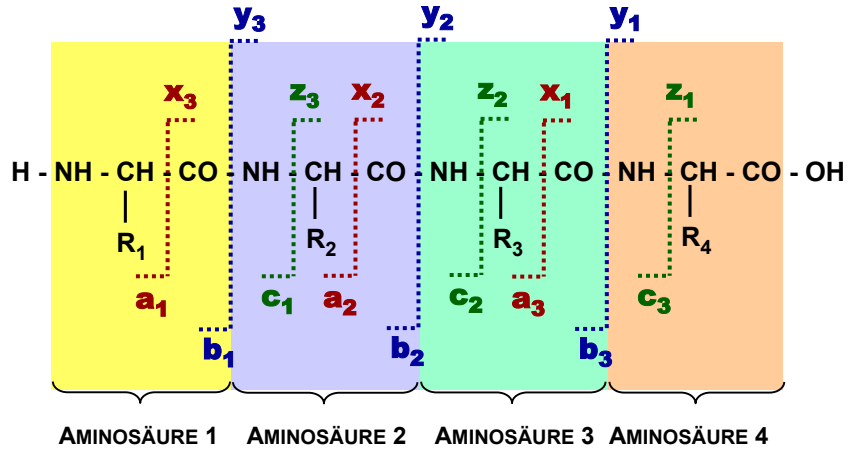


ISOLATION EINES VORLÄUFER-IONS (PEPTID)

ISOTOPENPEAKS

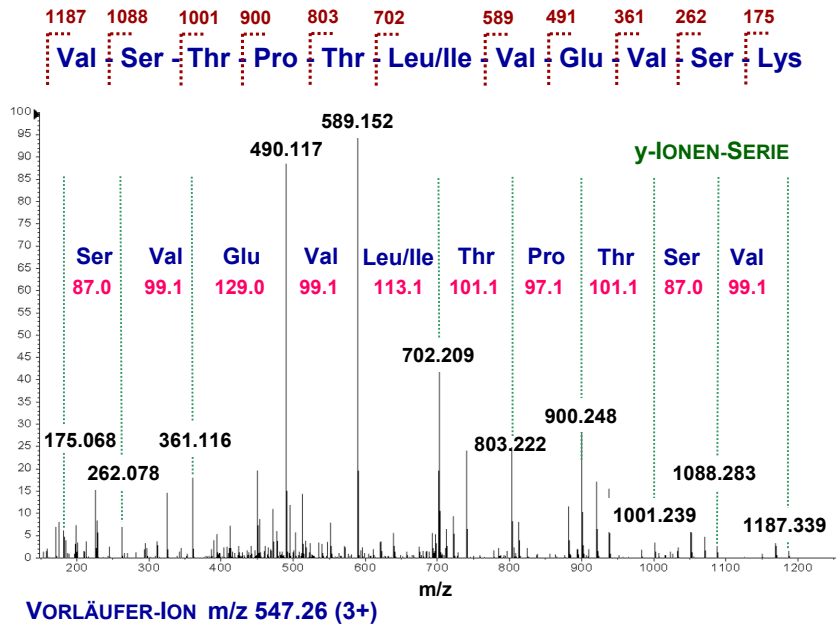


PEPTID-SEQUENZIERUNG MIT TANDEM-MS



(FAST) JEDE AMINOSÄURE HAT IHRE CHARAKTERISTISCHE MASSE

PEPTID-SEQUENZIERUNG MIT TANDEM-MS





CUPIENNIUS SALEI



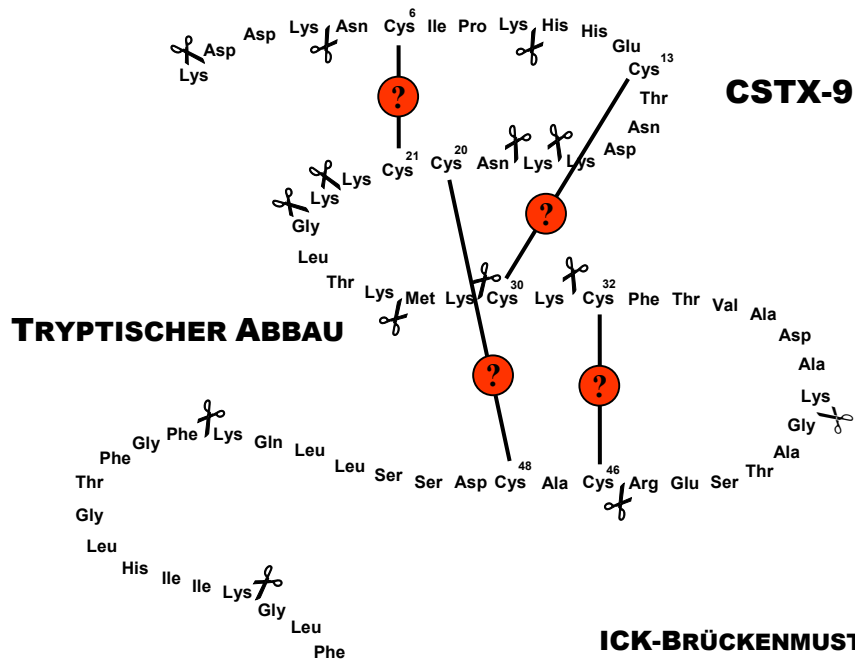
DAS GIFT VON *CUPIENNIUS SALEI*

- 8 - 12 µl TOXIN
PRO SPINNE UND MONAT
- HOHER SALZGEHALT
- FREIE AMINOSÄUREN
- PEPTIDE
 - ⇒ **CUPIENNINE**
 - 8 PEPTIDE
 - ~35 AMINOSÄUREN
 - KEINE DISULPHID-BRÜCKEN
 - ⇒ **CSTX - PEPTIDE**
 - CUPIENNIUS SALEI TOXINE**
 - 13 PEPTIDE
 - 65 - 78 AMINOSÄUREN
 - STARK VERKNOTETES BRÜCKENMUSTER

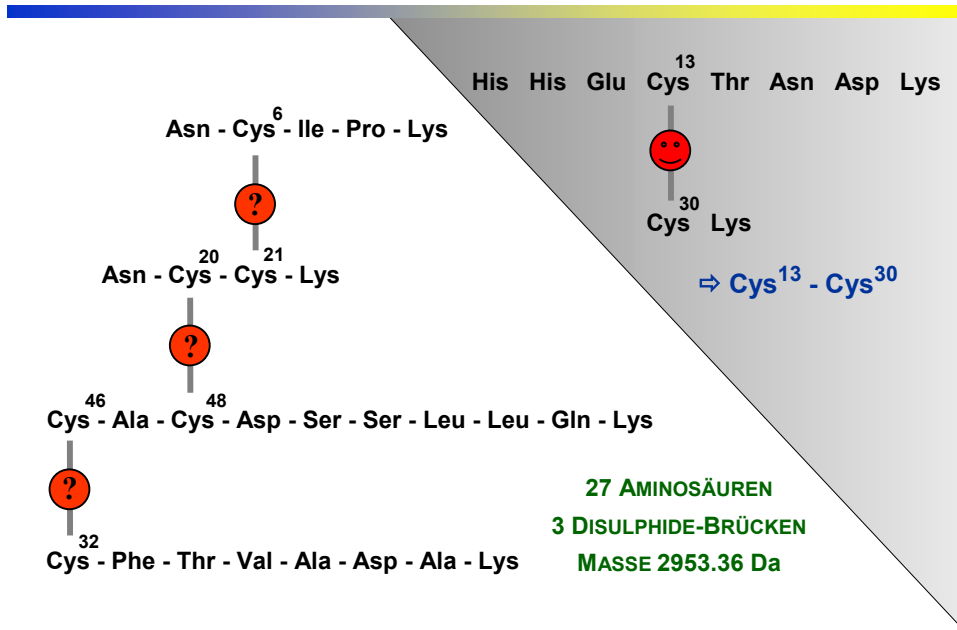


CSTX-PEPTIDE: AMINOSÄUREN-SEQUENZEN (EDMAN)

	10	20	
CSTX-1	S C I P K H E E C T N D K H N C C R K G L F		
CSTX-9	K D D K N C I P K H H E C T N D K K N C C K K G L T		
CSTX-13	S D C T L R N H D C T D D R H S C C R S K M F		
	30	40	50
CSTX-1	K L K C Q C S T F D D E S G Q P T E R C A C G R P		
CSTX-9	K M K C K C F T V A D A K G A T S E R C A C D S S		
CSTX-13	K D V C T C F Y P S Q C A K K E L C T C Q Q P		
	60	70	
CSTX-1	M G H Q A I E T G L N I F R G L F K G K K K N K K T K		
CSTX-9	L L Q K F G F T G L H I I K G L F		
CSTX-13	K H L K Y I E K G L Q K A K D Y A T		



**CSTX-9: CYSTINE-HALTIGE
FRAGMENTE AUS TRYPTISCHEM ABBAU**

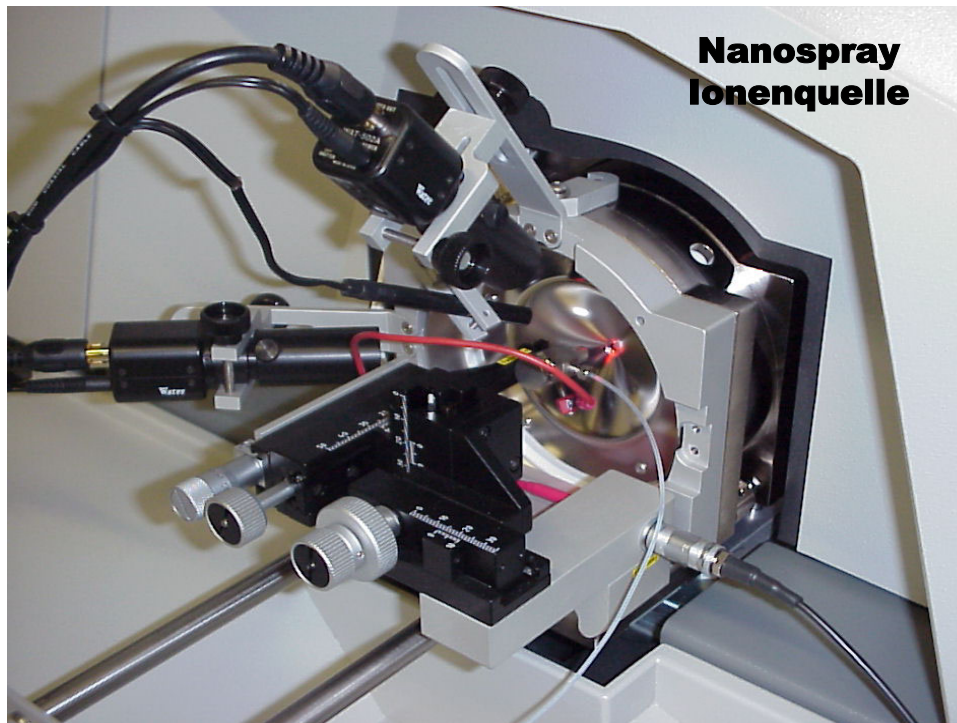
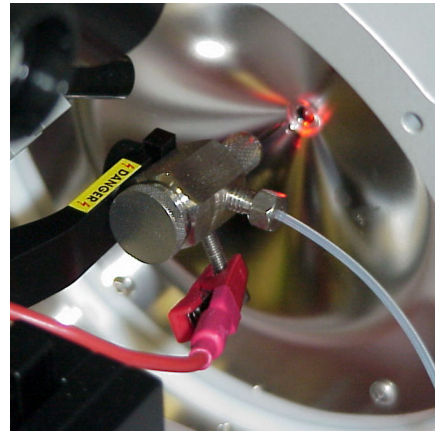
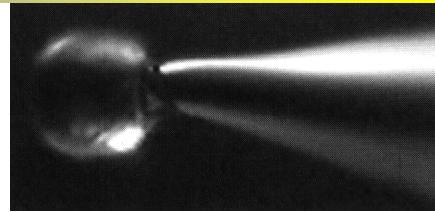


NANO-ELECTROSPRAY

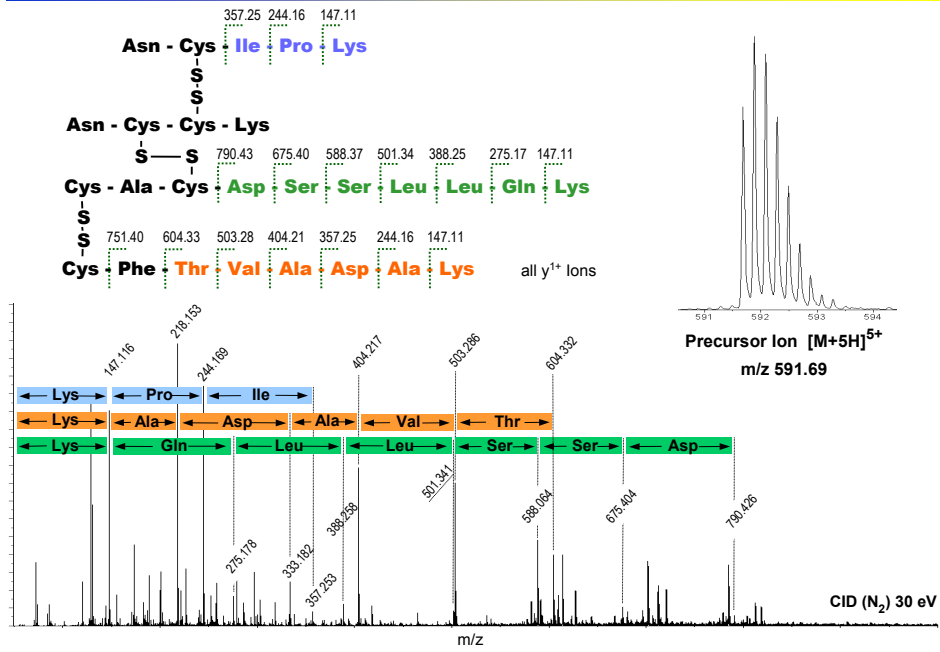
IONENQUELLE FÜR GERINGSTEN PROBENVERBRAUCH

- PROBENVOLUMEN 0.5 - 5 μ l
- FLUSSRATE 10-20 nl/min
- NADELÖFFNUNG \varnothing 1 μ m

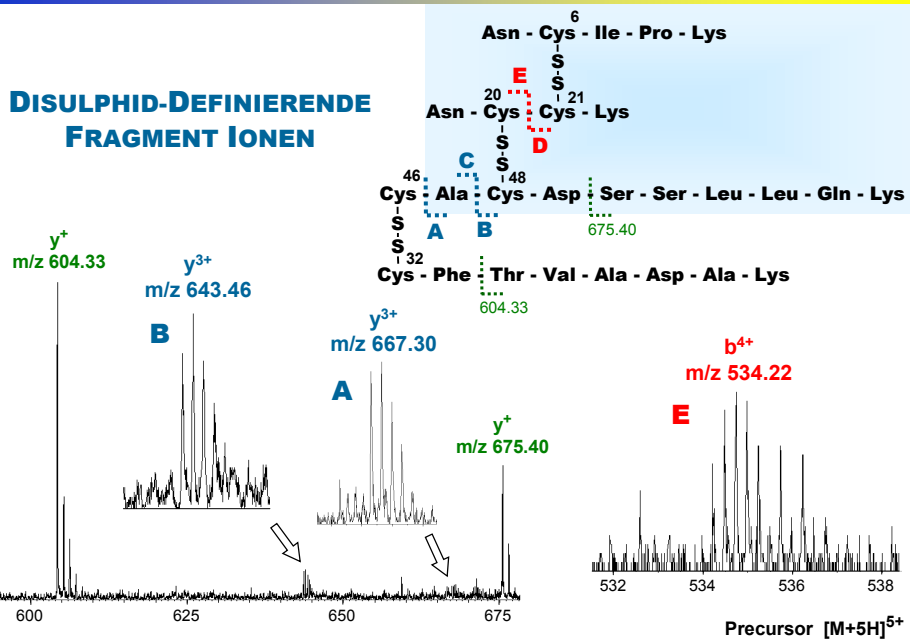
- MECHANISMUS WIE ESI
- EFFIZIENTE IONISIERUNG
- NUR OFF-LINE BETRIEB !



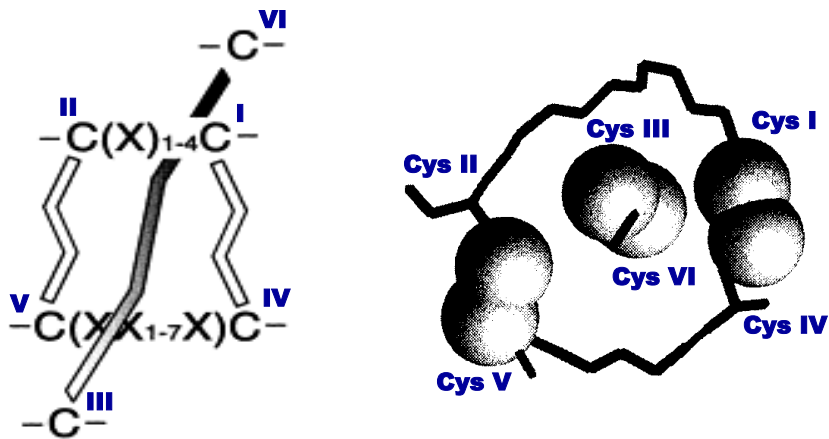
MS/MS DES TRYPTISCHEN CSTX-9 FRAGMENTS



MS/MS DES TRYPTISCHEN CSTX-9 FRAGMENTS



INHIBITOR CYSTINE KNOT (ICK) STRUCTURAL MOTIF



GENERELLE DISULPHID-ANORDNUNG IM ICK-MOTIV

Cys(I-IV) Cys(II-V) Cys(III-VI)

DANK

THE SPIDER PEOPLE

DR. LUZIA KUHN-NENTWIG
PROF. DR. WOLFGANG NENTWIG
BENNO WULLSCHLEGER

THE PROTEIN SEQUENCING PEOPLE

PD DR. JOHANN SCHALLER
URS KÄMPFER

THE OLIGONUCLEOTIDE PEOPLE

PROF. DR. CHRISTIAN LEUMANN
DR. ELOY BERNAL-MENDEZ

THE MASS SPEC PEOPLE

JAN TROMP
SELINA MONN
KAROL KROCKA
MARKUS STADLER