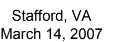
Training in Forensic DNA Analysis

Capillary Electrophoresis
(and microchip CE)
Fundamentals

Virginia Department of Forensic Science
Training Workshop

Stafford, VA
March 14, 2007



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Funding: Interagency Agreement 2003-IJ-R-029 between the National Institute of Justice and NIST Office of Law Enforcement Standards

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Stages of Technology for Forensic DNA Typing

- Idea
- Demonstration of feasibility
- Research and development
- Commercialization
- Validation by forensic labs
- Routine use by the community

Decision to Switch/Upgrade to New Technology

Hard to calculate

COST to Change

Improved Capabilities

Validation time & effort
Impact on legacy data

New multiplex STR kit
New detection technology
New DNA markers

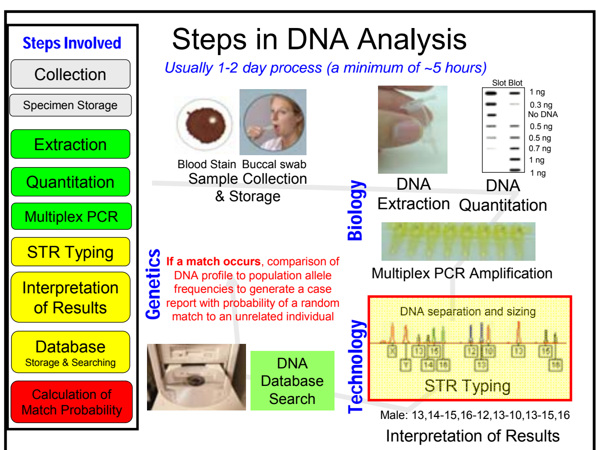
Decisions about Changing Technologies

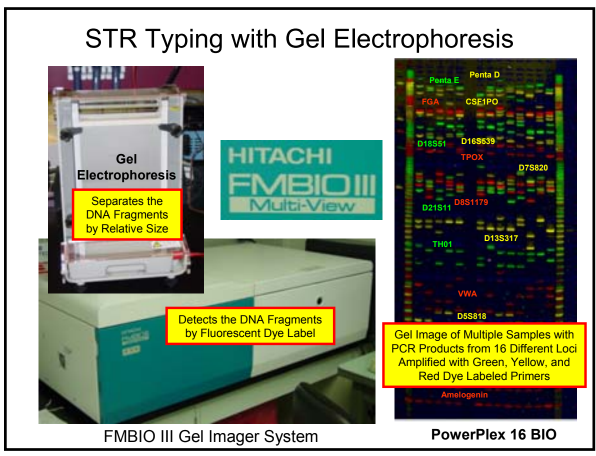
- Cost to change
- Comfort and experience levels
  - court approved methods must be used in forensic labs
- Capabilities…Enhancements
  - Are they really needed?
  - Will legacy data be impacted?

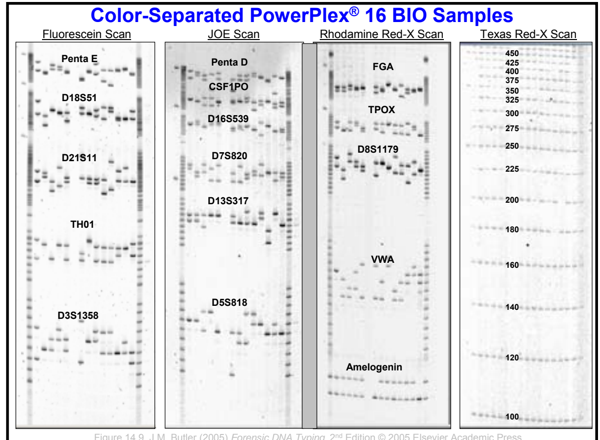
Where Is the Future Going for DNA Technology That Can Be Applied to Forensic DNA Typing?

Constant state of evolution (like computers)

- Higher levels of multiplexes
- More rapid DNA separations
- Better data analysis software
- New DNA Markers



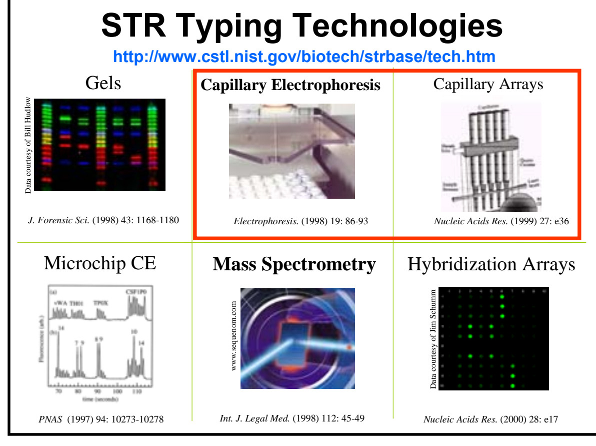


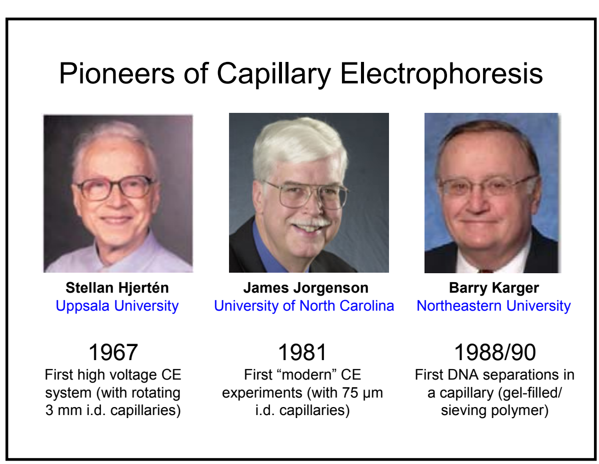


Presentation Outline

- History and background on CE
- Separation
- Injection and sample preparation
- Detection
- Microchip CE: similarities and differences

My Goal:
To help you understand the basic chemistry behind DNA separations and to help make CE instruments less of a "black box"





Stellan Hjertén

Uppsala University (Sweden)

With first fully automated capillary free zone electrophoresis apparatus in 1967

In 2003 at age 75

Received his PhD (1967) under Professor **Arne Tiselius** who had developed moving boundary zone electrophoresis in 1937 **(Noble Prize in 1948)**

A Brief History of Capillary Electrophoresis

- 1937 – Tiselius develops moving boundary electrophoresis
- 1967 – Hjertén uses rotating 3 mm i.d. tubes for CE
- **1981 – Jorgenson and Lukacs demonstrate first high performance CE separations with 75 µm i.d. capillary**
- 1988 – Karger's group shows DNA separations of single stranded oligonucleotides with gel-filled capillaries
- 1990 – Karger's group shows DNA separations with sieving polymers on DNA restriction fragments
- 1991 – Grossman expands work with sieving polymers
- 1992 – Bruce McCord starts working on PCR product separations with STR allelic ladders

My Experience with CE, STRs, etc.

- May 1993 – began working in Bruce McCord's lab at Quantico
- Sept 1993 – developed mtDNA amplicon quantitation method (used in FBI casework from 1996 to present)
- Nov 1993 – **first demonstration of STR typing by CE** (using dual internal standards and TH01 ladder)
- July 1995 – defended Ph.D. dissertation entitled "Sizing and Quantitation of Polymerase Chain Reaction Products by Capillary Electrophoresis for Use in DNA Typing"
- July 1995 – ABI 310 Genetic Analyzer was released

My Experience with CE, STRs, etc. (cont.)

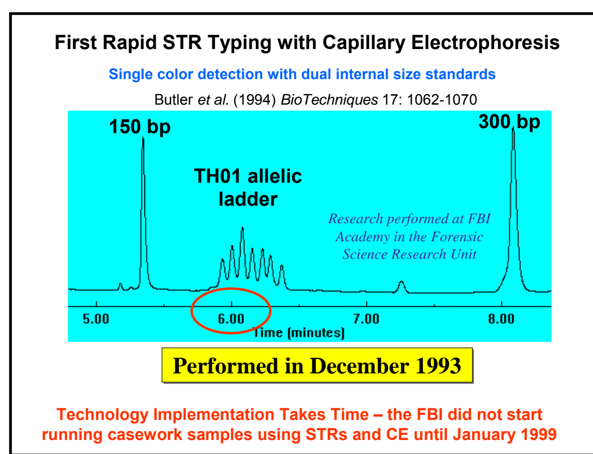
- 1996-1997 Developed STRBase while a postdoc at NIST
- Nov 1998 – GeneTrace Systems purchased a 310; typed several hundred samples with Profiler Plus and Cofiler kits and compared results to mass spec STR analysis
- **1999-present – Run thousands of samples with all STR kits available (except PP 1.2) and developed a number of new STR multiplex systems**
- Jan 2001 – Published "*Forensic DNA Typing: Biology and Technology behind STR Markers*" (2nd Edition in Feb 2005)
- April 2001-present – Use of ABI 3100 16-capillary array system

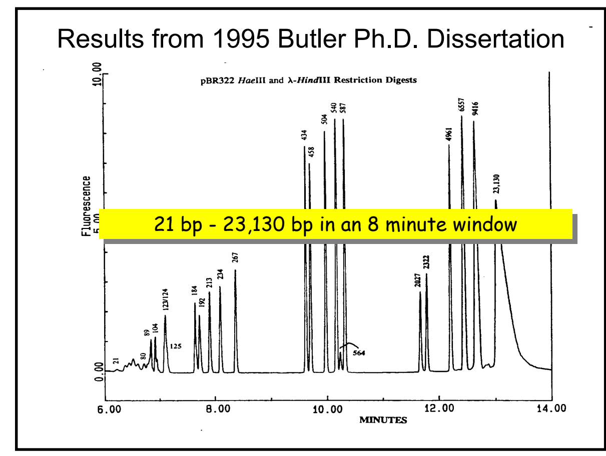
In the early 1990s the real question was how to transition from a gel to a capillary

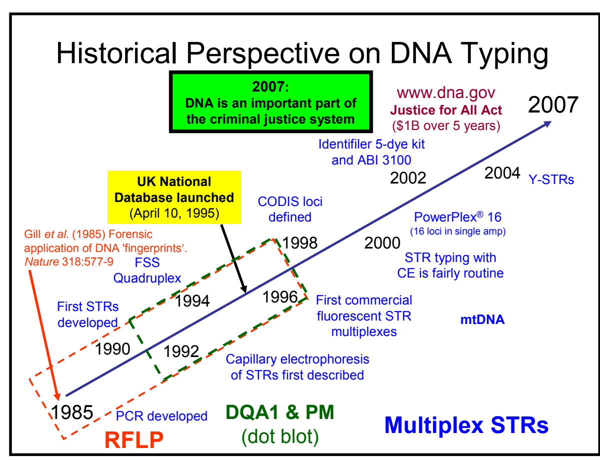
- Cross-linked acrylamide gel filled capillaries were tried first
  - Reusable?
  - Bubble formation
  - Themal degradation
- Alternative was to not use a gel at all
  - Refillable sieving polymers
  - However, resolution was poor early on

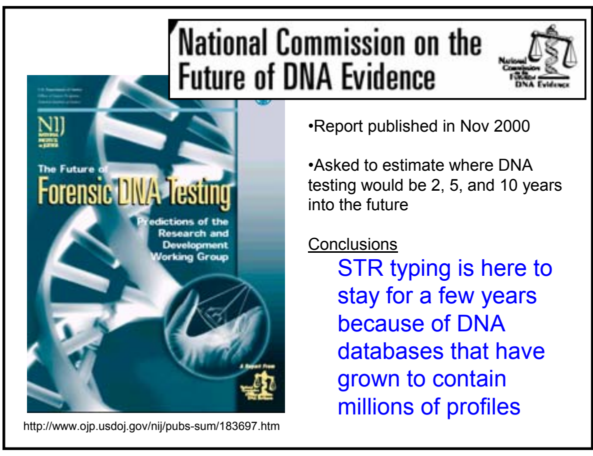
Early Work with CE and STRs

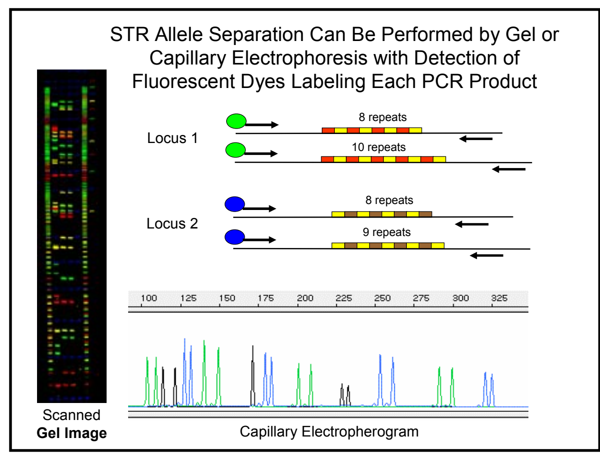
- Barry Karger's group (1988-1990)
  - Utilized gel-filled capillaries to separate ssDNA
  - Introduced sieving polymers in the form of linear polyacrylamide to separate restriction digests
- Beckman P/ACE 2050 is introduced in 1992 as the first commercially available CE coupled to a laser to enable fluorescence detection
- John Butler and Bruce McCord (1993-1995)
  - **First STR typing with single color CE using intercalating dyes and dual bracketing internal size standards**
- Rich Mathies' group (1995)
  - First STR typing with multi-color CE (and multi-capillary) using dye-labeled primers
- **ABI 310 is introduced in July 1995 as the first commercially available multi-color CE**









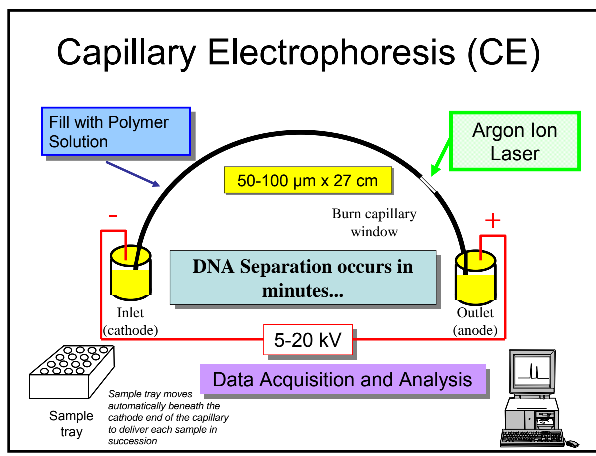


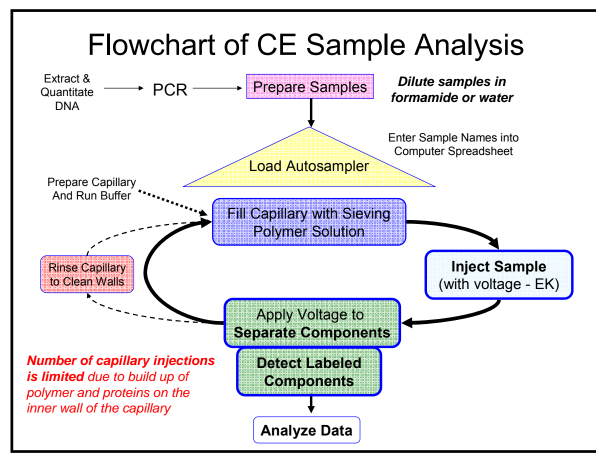
Why Use CE for DNA Analysis?

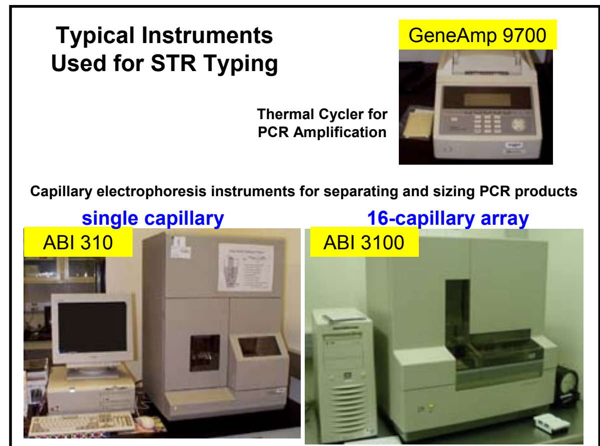
1. Injection, separation, and detection are automated.
2. Rapid separations are possible
3. Excellent sensitivity and resolution
4. The time at which any band elutes is precisely determined
5. Peak information is automatically stored for easy retrieval

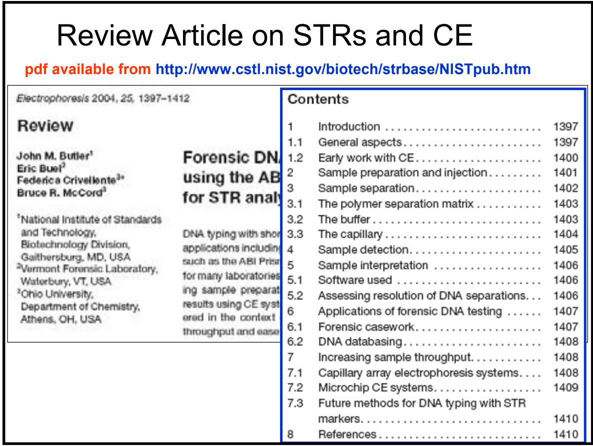
Gels

Symbol first used in Oct 1994 at the Promega meeting when I had a poster introducing the use of CE for STR typing









Electrophoresis 2004, 25, 1397–1412

Review

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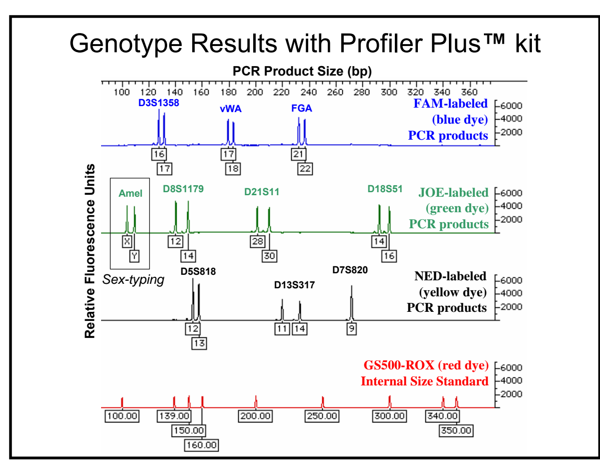
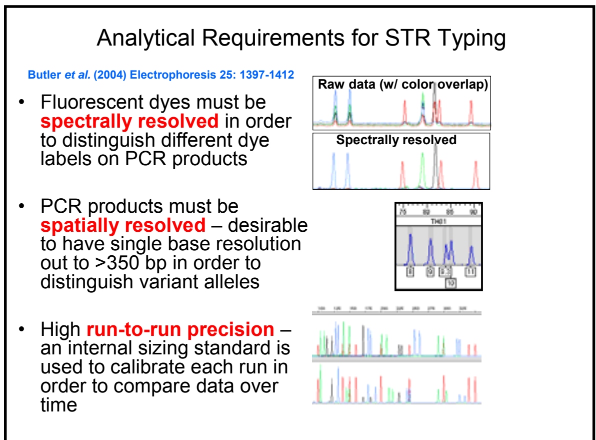
Forensic DN[A] using the AB[I] for STR anal[ysis]

DNA typing with sho[rt]... applications includin[g]... such as the ABI Pris[m]... for many laboratorie[s]... ing sample preparat[ion]... results using CE syst[ems]... ered in the context... throughput and ease...

Contents

1 Introduction . . . 1397
1.1 General aspects . . . 1397
1.2 Early work with CE . . . 1400
2 Sample preparation and injection . . . 1401
3 Sample separation . . . 1402
3.1 The polymer separation matrix . . . 1403
3.2 The buffer . . . 1403
3.3 The capillary . . . 1404
4 Sample detection . . . 1405
5 Sample interpretation . . . 1406
5.1 Software used . . . 1406
5.2 Assessing resolution of DNA separations . . . 1406
6 Applications of forensic DNA testing . . . 1407
6.1 Forensic casework . . . 1407
6.2 DNA databasing . . . 1408
7 Increasing sample throughput . . . 1408
7.1 Capillary array electrophoresis systems . . . 1408
7.2 Microchip CE systems . . . 1409
7.3 Future methods for DNA typing with STR markers . . . 1410
8 References . . . 1410





Important Differences Between CE and Gels

- **Room temperature control** is essential for run-to-run precision
  - CE uses sequential rather than simultaneous separations
  - Usually need < ±0.2 °C (must inject allelic ladder regularly)
- **Lower amount of DNA loaded** (injection = nL vs µL) and thus detection sensitivity must be better
- Electrokinetic injection enables **dye artifacts** (blobs) to enter the capillary or microchip CE channel and thus possibly interfere with STR allele interpretation

More Differences between CE and Gels…

- Filling the capillary (or microchip CE channel) is analogous to pouring a gel into a tiny tube…
- Must be more clean around a CE system
  - Because the capillaries (µCE channels) are small, particles of dust or urea crystals can easily plug them
  - Tips of capillary cannot dry out (once buffer solutions have been run through them) for the same reasons
- Bubbles are a BIG problem in CE as they can easily block current flow in the capillary…

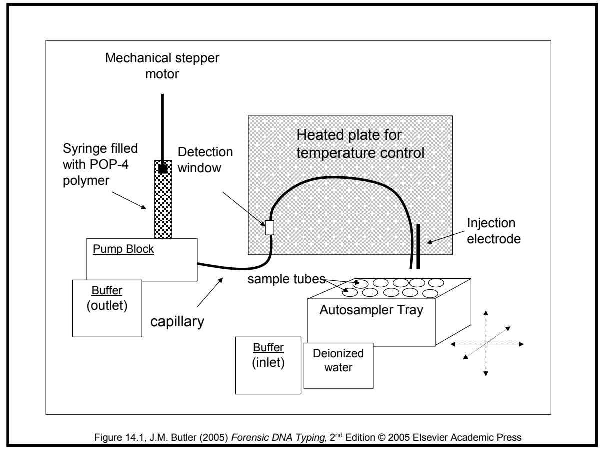
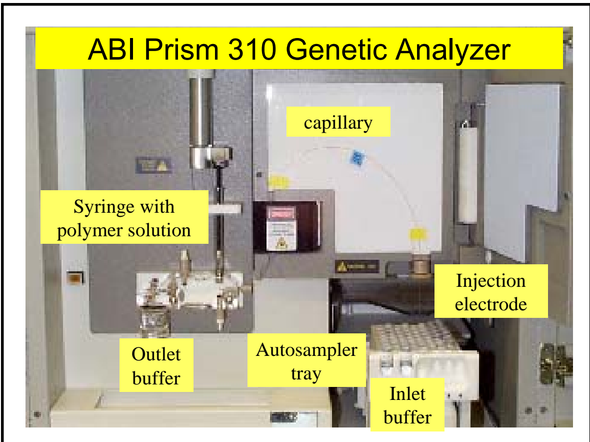
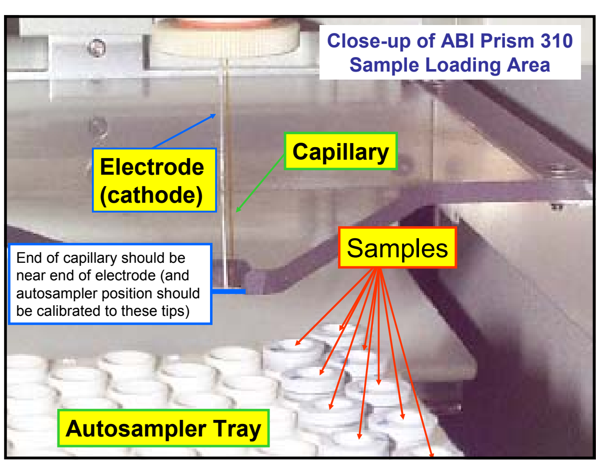
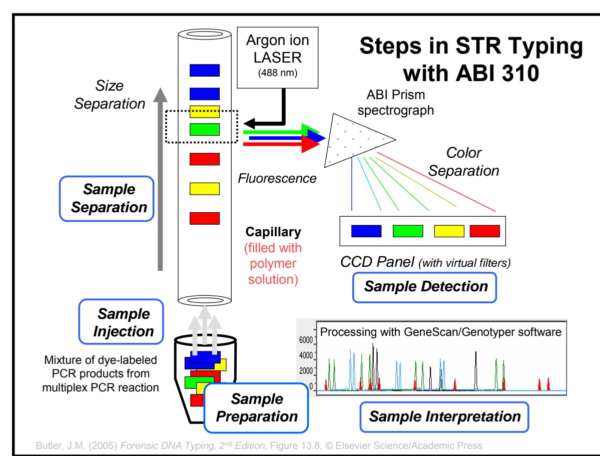


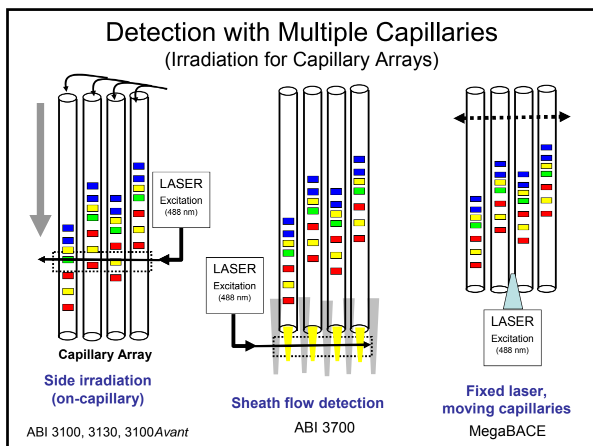
Figure 14.1, J.M. Butler (2005) *Forensic DNA Typing*, 2nd Edition © 2005 Elsevier Academic Press







Butler, J.M. (2005) *Forensic DNA Typing*, 2nd Edition, Figure 13.8, © Elsevier Science/Academic Press



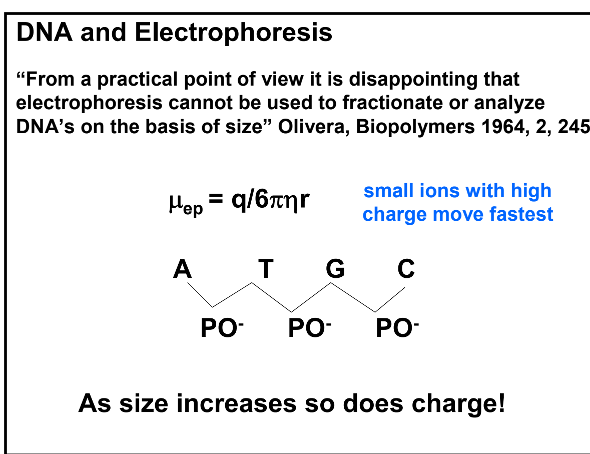
Process Involved in 310/3100 Analysis

- Separation
  - Capillary – 50um fused silica, 43 cm length (36 cm to detector)
  - POP-4 polymer – Polydimethyl acrylamide
  - Buffer - TAPS pH 8.0
  - Denaturants – urea, pyrolidinone
- Injection
  - electrokinetic injection process (formamide, water)
  - importance of sample stacking
- Detection
  - fluorescent dyes with excitation and emission traits
  - CCD with defined virtual filters produced by assigning certain pixels

Separation

Ohm's Law

- V = IR (where V is voltage, I is current, and R is resistance)
- Current, or the flow of ions, is what matters most in electrophoresis
- CE currents are much lower than gels because of a higher resistance in the narrow capillary
- CE can run a higher voltage because the capillary offers a higher surface area-to-volume ratio and can thus dissipate heat better from the ion flow (current)



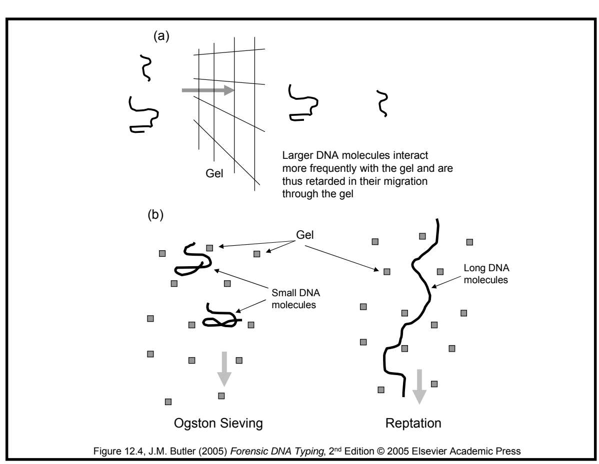


Figure 12.4, J.M. Butler (2005) *Forensic DNA Typing*, 2nd Edition © 2005 Elsevier Academic Press

Separation Issues

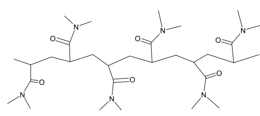
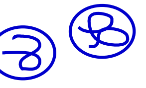
- Electrophoresis buffer –
  - Urea for denaturing and viscosity
  - Buffer for consistent pH
  - Pyrolidinone for denaturing DNA
  - EDTA for stability and chelating metals
- Polymer solution -- POP-4 (but others work also)
- Capillary wall coating -- dynamic coating with polymer
  - Wall charges are masked by methyl acrylamide
- Run temperature -- 60 °C helps reduce secondary structure on DNA and improves precision. (Temperature control affects DNA sizing)

DNA Separations in Entangled Polymer Sieving Solutions

- Size based separation due to interaction of DNA molecules with entangled polymer strands
- Polymers are not cross-linked (as in slab gels)
- "Gel" is not attached to the capillary wall
- Pumpable -- can be replaced after each run
- Polymer length and concentration determine the separation characteristics

Entangled Polymer Solutions

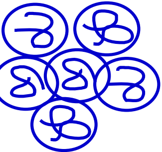
- Polymers are not cross-linked (above entanglement threshold)
- "Gel" is not attached to the capillary wall
- Pumpable -- can be replaced after each run
- Polymer length and concentration determine the separation characteristics
- Examples:
  - 1% HEC (hydroxyethyl cellulose)
  - 4% polyvinyl pyrolidinone
  - POP-4 and POP-6

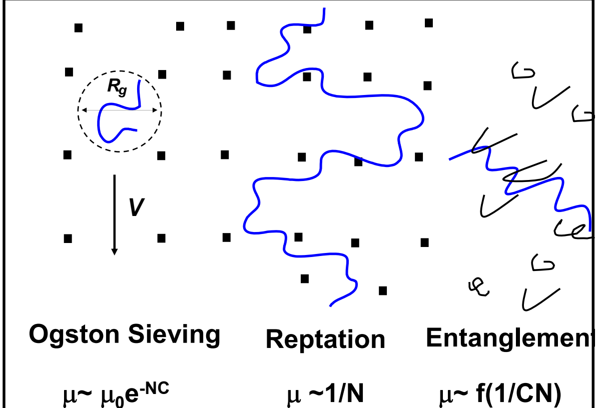
POP4 Polymer

Polydimethyl acrylamide

Transient Pores Are Formed Above the Entanglement Threshold.



*C < C**　　*C = C**　　*C > C**



What is in POP-4 and Genetic Analyzer Buffer?

© 1997 Oxford University Press　Nucleic Acids Research, 1997, Vol. 25, No. 19　3925–3929

Improved single-strand DNA sizing accuracy in capillary electrophoresis

Barnett B. Rosenblum*, Frank Oaks, Steve Menchen and Ben Johnson

PE Applied Biosystems, 850 Lincoln Centre Drive, Foster City, CA 94404, USA

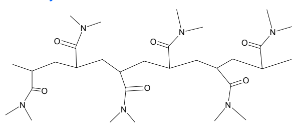
Received May 29, 1997; Revised and Accepted August 6, 1997

See also Wenz *et al.* (1998) *Genome Research* 8: 69-80

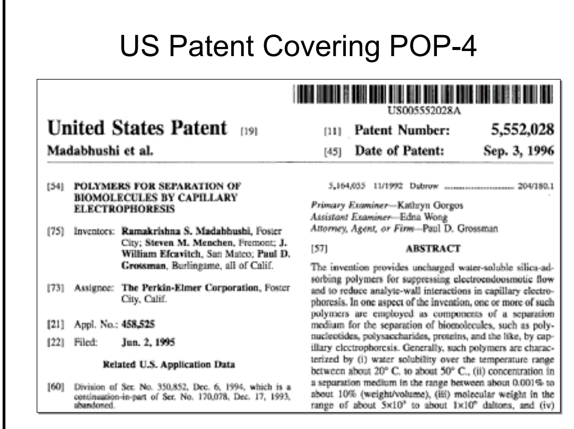
POP-4 (4% poly-dimethylacrylamide, 8 M urea, 5% 2-pyrrolidinone)

US Patent 5,552,028 covers POP-4 synthesis

Running buffer contains 100 mM TAPS and 1 mM EDTA (adjusted to pH 8.0 with NaOH) *TAPS = N-Tris-(hydroxymethyl)methyl-3-aminopropane-sulfonic acid*



US Patent Covering POP-4



US005552028A

United States Patent [19]
Madabhushi et al.

[11] **Patent Number:** 5,552,028
[45] **Date of Patent:** Sep. 3, 1996

[54] POLYMERS FOR SEPARATION OF BIOMOLECULES BY CAPILLARY ELECTROPHORESIS

[75] Inventors: Ramakrishna S. Madabhushi, Foster City; Steven M. Menchen, Fremont; J. William Efcavitch, San Mateo; Paul D. Grossman, Burlingame, all of Calif.

[73] Assignee: The Perkin-Elmer Corporation, Foster City, Calif.

[21] Appl. No.: 458,525

[22] Filed: Jun. 2, 1995

Related U.S. Application Data

[60] Division of Ser. No. 350,852, Dec. 6, 1994, which is a continuation-in-part of Ser. No. 170,078, Dec. 17, 1993, abandoned.

5,164,055 11/1992 Dubrow 204/180.1

Primary Examiner—Kathryn Gorgos
Assistant Examiner—Edna Wong
Attorney, Agent, or Firm—Paul D. Grossman

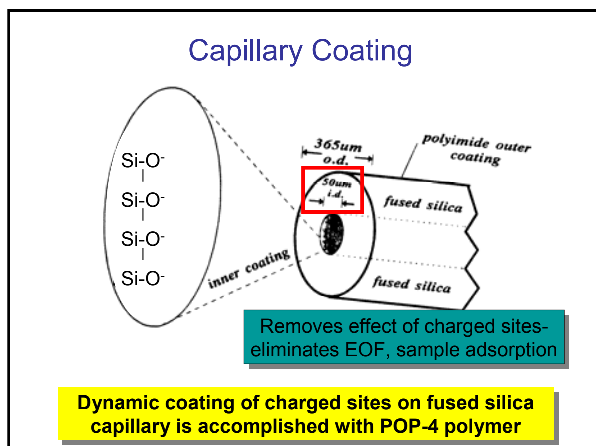
[57] ABSTRACT

The invention provides uncharged water-soluble silica-adsorbing polymers for suppressing electroendoosmotic flow and to reduce analyte-wall interactions in capillary electrophoresis. In one aspect of the invention, one or more of such polymers are employed as components of a separation medium for the separation of biomolecules, such as polynucleotides, polysaccharides, proteins, and the like, by capillary electrophoresis. Generally, such polymers are characterized by (i) water solubility over the temperature range between about 20° C. to about 50° C., (ii) concentration in a separation medium in the range between about 0.001% to about 10% (weight/volume), (iii) molecular weight in the range of about 5×10³ to about 1×10⁶ daltons, and (iv)

Why TAPS instead of Tris-borate (TBE) buffer?

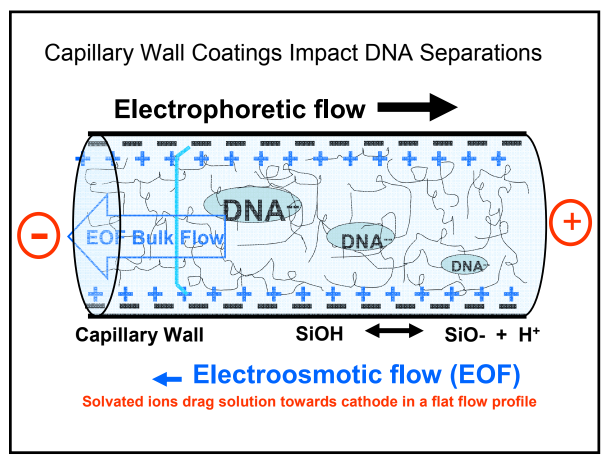
- TBE is temperature/pH sensitive
  - as temperature increases, the pH decreases (0.02 pH units with every 1 °C); this is the principle by which TaqGold activation works
- At lower pH, fluorescence emission of dyes decreases
  - see Singer and Johnson (1997) *Proceedings of the Eighth International Symposium on Human Identification*, pp. 70-77
- Thus when running at 60 °C on the ABI 310, if Tris-borate was used, fluorescent intensity of PCR products would be lower

Capillary Coating



Dynamic coating of charged sites on fused silica capillary is accomplished with POP-4 polymer

Capillary Wall Coatings Impact DNA Separations

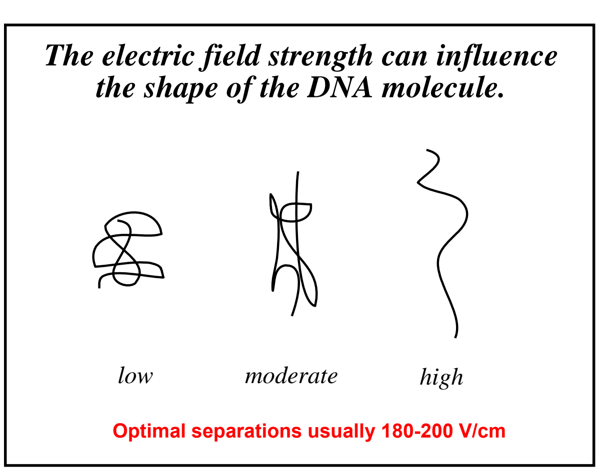


How to Improve Resolution?

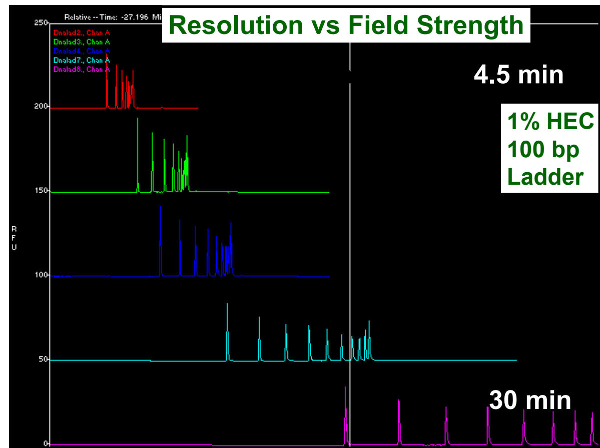
1. Lower Field Strength
2. Increase Capillary Length
3. Increase Polymer Concentration
4. Increase Polymer Length

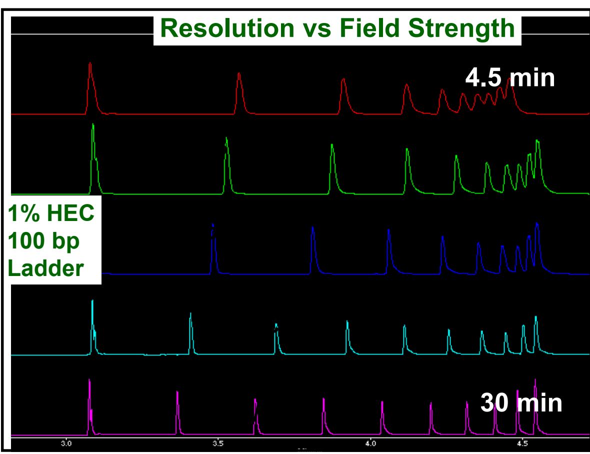
All of these come at a cost of longer separation run times

The electric field strength can influence the shape of the DNA molecule.

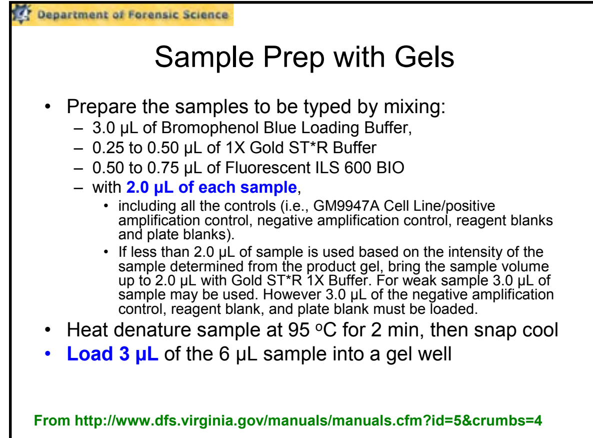


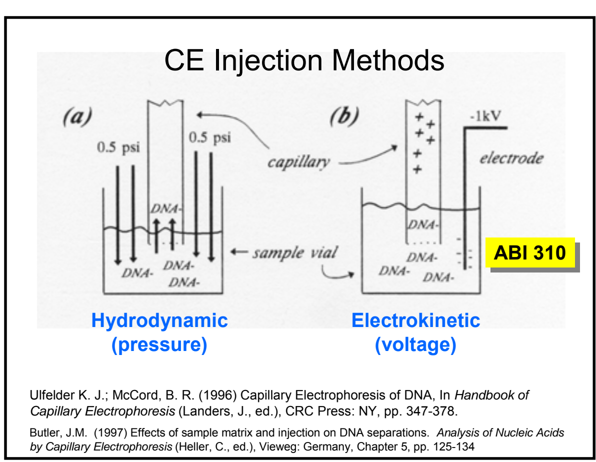
Optimal separations usually 180-200 V/cm

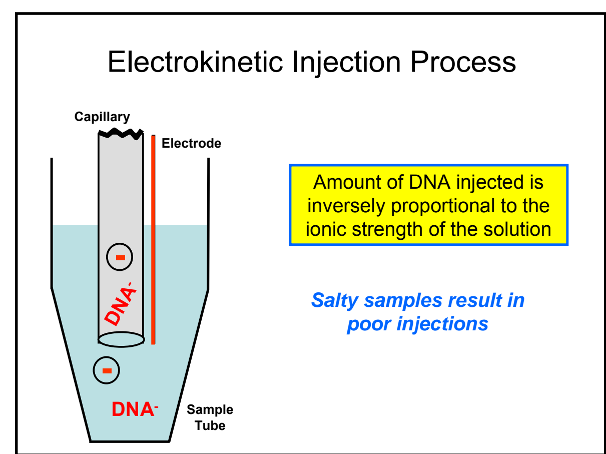


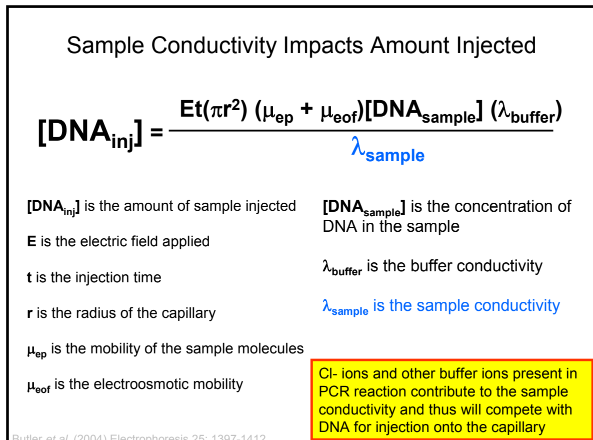


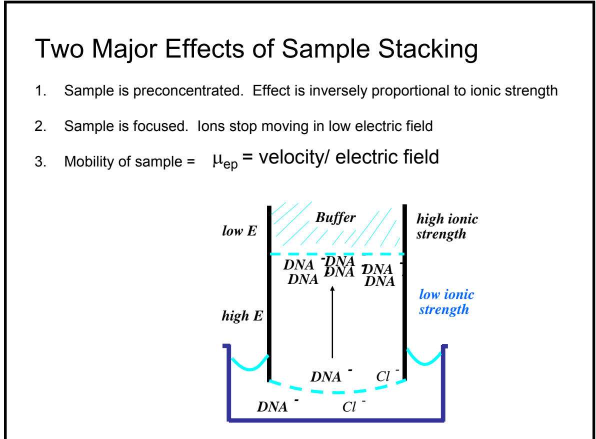
Injection











Steps Performed in Standard Module

See J.M. Butler (2005) *Forensic DNA Typing*, 2nd Edition; Chapter 14

- **Capillary fill** – polymer solution is forced into the capillary by applying a force to the syringe
- **Pre-electrophoresis –** the separation voltage is raised to 10,000 volts and run for 5 minutes;
- **Water wash of capillary – capillary is dipped several times in deionized water to remove buffer salts that would interfere with the injection process**
- **Sample injection** – the autosampler moves to position A1 (or the next sample in the sample set) and is moved up onto the capillary to perform the injection; a voltage is applied to the sample and a few nanoliters of sample are pulled onto the end of the capillary; the default injection is 15 kV (kilovolts) for 5 seconds
- **Water wash of capillary** – capillary is dipped several times in waste water to remove any contaminating solution adhering to the outside of the capillary
- **Water dip** – capillary is dipped in clean water (position 2) several times
- **Electrophoresis** – autosampler moves to inlet buffer vial (position 1) and separation voltage is applied across the capillary; the injected DNA molecules begin separating through the POP-4 polymer solution
- **Detection** – data collection begins; raw data is collected with no spectral deconvolution of the different dye colors; the matrix is applied during Genescan analysis

Typical Sample Preparation for ssDNA

1. Perform PCR with dye-labeled primers
2. Dilute 1 μL PCR product with 24 μL **deionized formamide**; add 1 μL ROX-labeled internal sizing standard
3. Denature 2 minutes at 95 °C with thermocycler
4. Cool to 4 °C in thermocycler or ice bath
5. Sample will remain denatured for at least 3 days

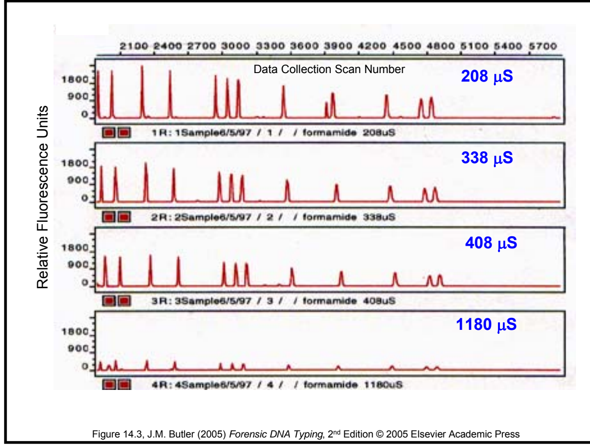


Figure 14.3, J.M. Butler (2005) *Forensic DNA Typing*, 2nd Edition © 2005 Elsevier Academic Press

Comments on Sample Preparation

- Use high quality formamide (<100 µS/cm)!
  - ABI sells Hi-Di formamide
  - regular formamide can be made more pure with ion exchange resin
- Deionized water vs. formamide
  - Biega and Duceman (1999) *J. Forensic Sci.* 44: 1029-1031
  - *Crivellente, Journal of Capillary Electrophoresis* **2002,** *7 (3-4)*, 73-80.
  - water works fine but samples are not stable as long as with formamide; water also evaporates over time…
- Denaturation with heating and snap cooling
  - use a thermal cycler for heating and cold aluminum block for snap cooling
  - heat/cool denaturation step is necessary only if water is substituted for formamide...

January 6, 2005 Letter from Applied Biosystems to ABI 310 Customers

- "Testing has shown that Hi-Di Formamide denatures DNA **without the need to heat samples**…"
- In other words, no heat denaturation and snap cooling needed!

Applied Biosystems Okays Use of Deionized Water for DNA Sequencing

Technical Bulletin #1 **Issued August 2006**

Applied Biosystems 3730/3730*xl* DNA Analyzer

Subject: Influence of Sequencing Injection Solution on 3730/3730xl DNA Analyzer Performance

In this Bulletin:

- Three Loading Solutions Tested on Page 1
- Loading Solution Test Data on Page 2
- Recommendations on Page 6
- Guidelines for Use on Page 6

Three Loading Solutions Tested

Loading Solution Background

Applied Biosystems presently recommends the use of Hi-Di™ Formamide as the sample-loading solution for all Applied Biosystems DNA sequencers to ensure sample preservation and resistance to evaporation. However, many users of the 3730 choose either deionized water or dilute EDTA solutions. These choices are driven largely by cost and safety/hazardous material considerations.

Detection

Detection Issues

- Fluorescent dyes
  - spectral emission overlap
  - relative levels on primers used to label PCR products
  - dye "blobs" (free dye)
- Virtual filters
  - hardware (CCD camera)
  - software (color matrix)

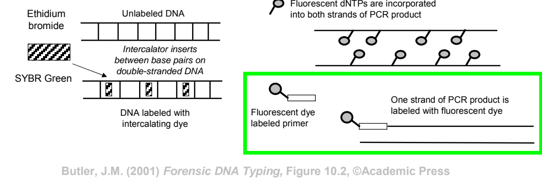
Filters determine which wavelengths of light are collected onto the CCD camera

Laser Used in ABI 310

- Argon Ion Laser
- 488 nm and 514.5 nm for excitation of dyes
- 10 mW power
- Lifetime ~5,000 hours (1 year of full-time use)
- Cost to replace ~$5,500
- Leads to highest degree of variability between instruments and is most replaced part
- Color separation matrix is specific to laser used on the instrument

Methods for Fluorescently Labeling DNA

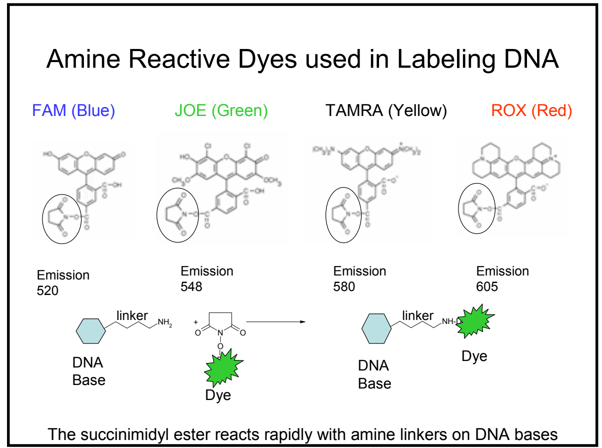
- Intercalating Dyes (post-PCR)
- Dye-labeled nucleotide insertion during PCR
- Dye-labeled primer insertion during PCR

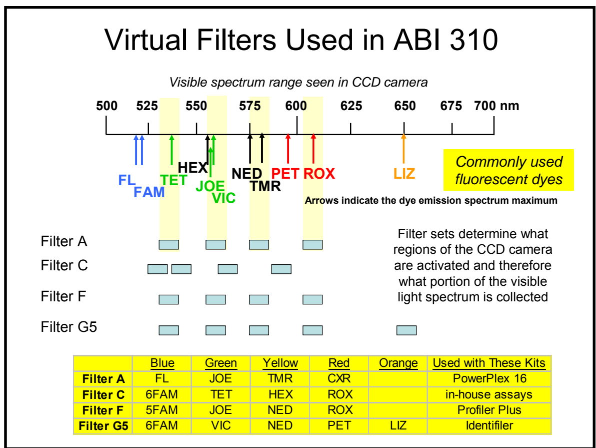


Butler, J.M. (2001) *Forensic DNA Typing*, Figure 10.2, ©Academic Press

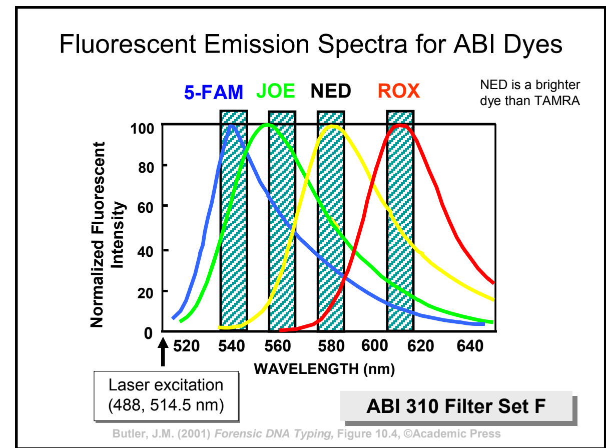
Fluorescent Labeling of PCR Products

- Dyes are attached to one primer in a pair used to amplify a STR marker
- Dyes are coupled to oligonucleotides (primers) through NHS-esters and amine linkages on the 5'end of the primer: Dye-$(CH_2)_6$-primer
- Dye-labeled oligonucleotides are incorporated during multiplex PCR amplification giving a specific color "tag" to each PCR product
- PCR products are distinguished using CCD imaging on the 310





	Blue	Green	Yellow	Red	Orange	Used with These Kits
Filter A	FL	JOE	TMR	CXR		PowerPlex 16
Filter C	6FAM	TET	HEX	ROX		in-house assays
Filter F	5FAM	JOE	NED	ROX		Profiler Plus
Filter G5	6FAM	VIC	NED	PET	LIZ	Identifiler

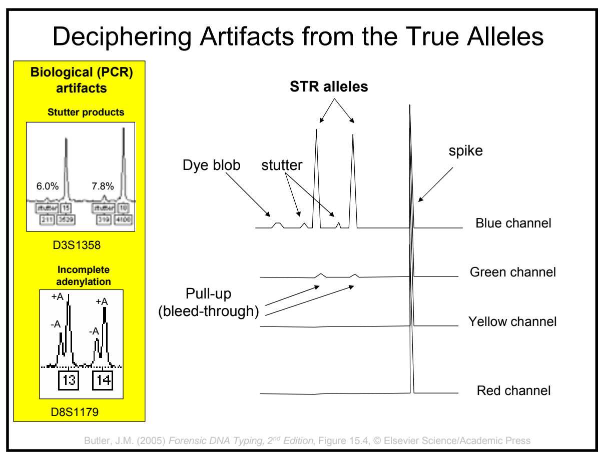


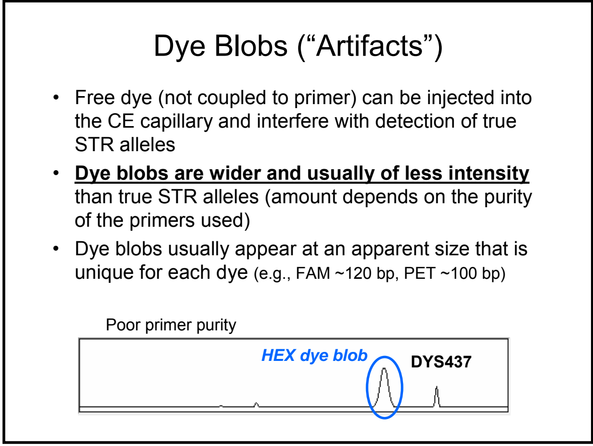
Please Note!

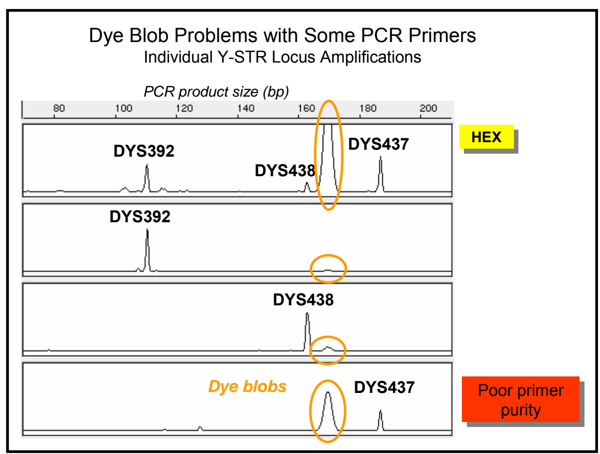
- There are no filters in a 310
- Its just the choice of pixels in the CCD detector
- All the light from the grating is collected
- You just turn some pixels on and some off

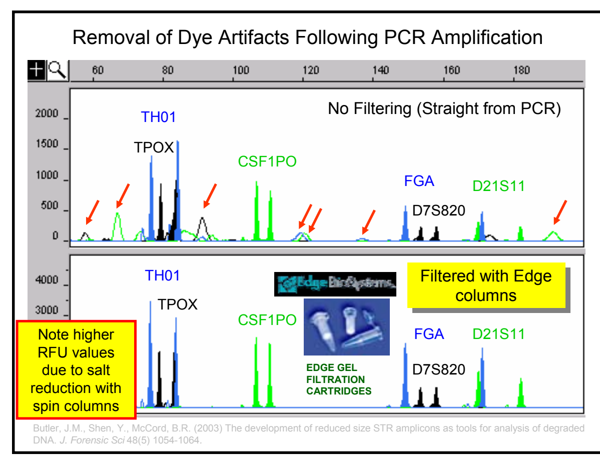
Comments on Matrices/Spectral Calibration (Multi-Component Analysis)

- Make sure that the right filter set and matrix are applied when collecting data
- You can always apply another matrix to a sample collected on the ABI 310 but it must be run with the right filter set (matrix must be run first with ABI 3100)
- It is important to update matrices on a regular basis (depending on use) due to differences in laser power over time
- A good indication of when to run a new matrix is the observation of pull-up between dye colors when peaks are smaller than ~4,000 RFUs









Conclusions

DNA typing by capillary electrophoresis involves:

1) The use of entangled polymer buffers
2) Injection by sample stacking
3) Multichannel laser induced fluorescence
4) Internal and external calibration

Practical Aspects of ABI 310/3100 Use

ABI Genetic Analyzer Usage at NIST

- ABI 310 x 2 (originally with Mac, then NT)
  - 1st was purchased in 1996
  - 2nd was purchased in June 2002
- ABI 3100 (Data collection v1.0.1)
  - Purchased in June 2002
  - Original data collection software retained

Jan 2007 – upgraded to 3130xl with data collection v3.0

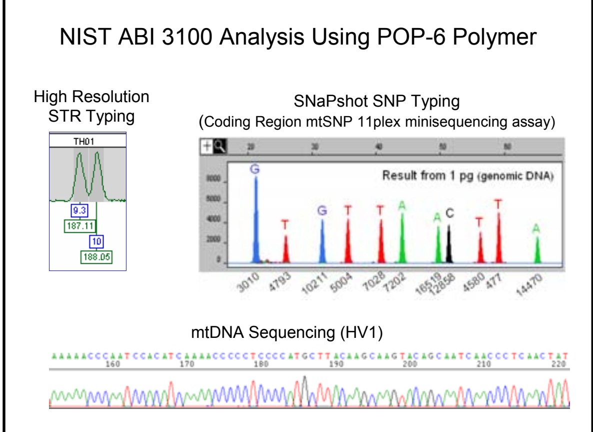
- ABI 3130xl upgrade (Data collection v3.0)
  - Purchased in April 2001 as ABI 3100
  - Upgraded to ABI 3130xl in September 2005
  - Located in a different room

Our Use of the ABI 3100

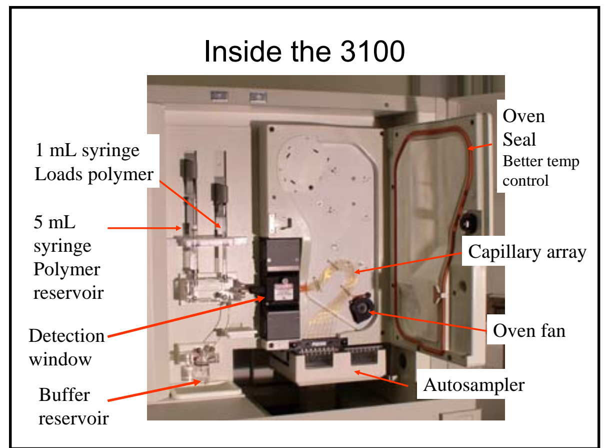
- Data collection software, version 1.0.1
- **POP-6** with 36 cm capillary array
- STR kits and in-house assays for autosomal STRs, Y-STRs, and miniSTRs
- SNaPshot assays for mtDNA SNPs, Y-SNPs, and autosomal SNPs
- DNA sequencing for mtDNA and STR repeat sequencing

We can routinely get more than 400 runs per capillary array by not changing the polymer between applications

NIST ABI 3100 Analysis Using POP-6 Polymer

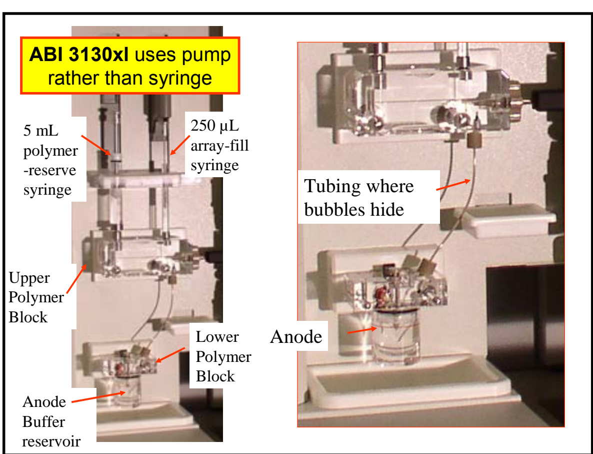


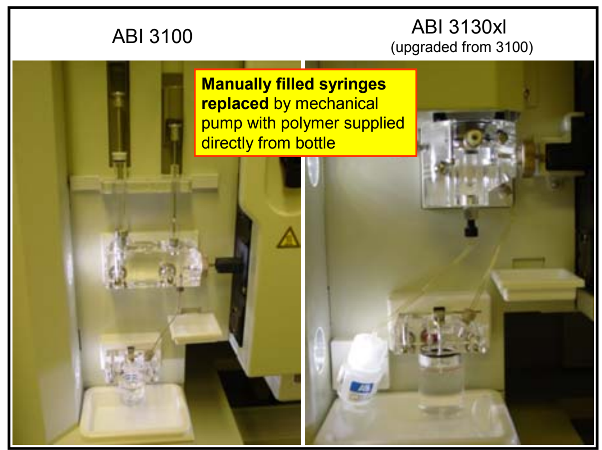
Inside the 3100

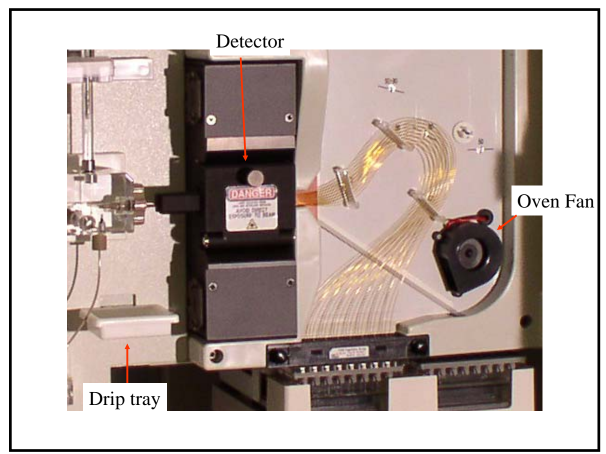


ABI 3100 and 3130xl Differences

- Polymer Block
  - No more manually filled syringes for the 3130xl
- Polymer solution
  - POP-7 vs. POP-4 and POP-6
- Data Collection software
  - New, user-friendly features in the upgraded software
  - Compensation for the red dye channel (variable binning – not present in v1.0.1)







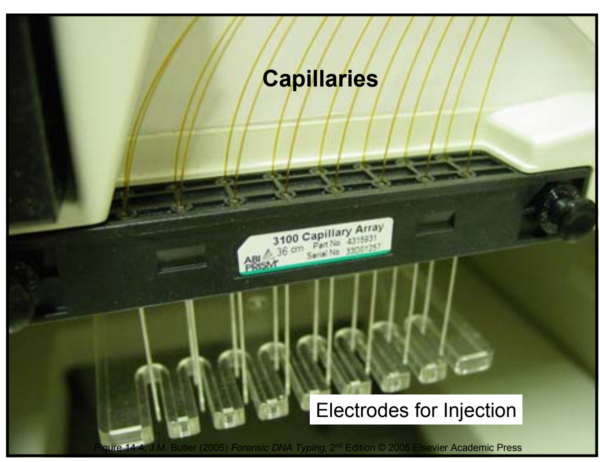
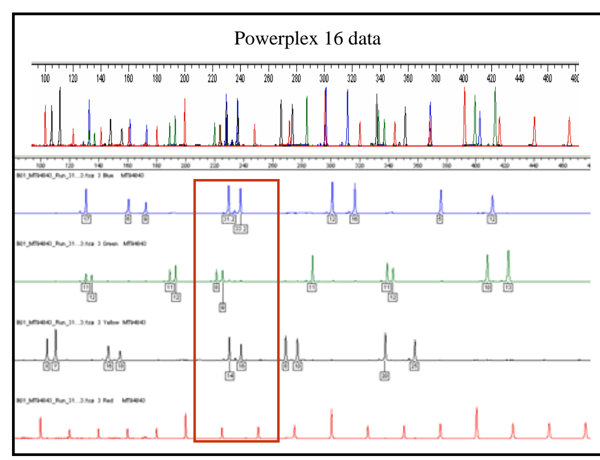
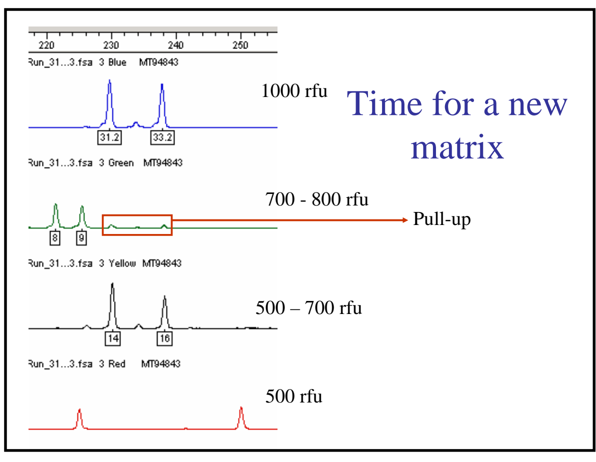
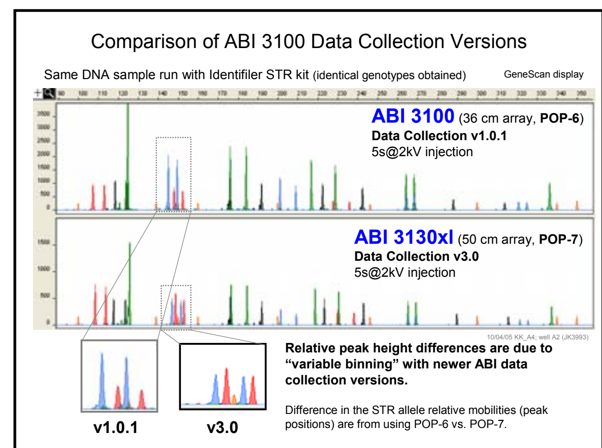


Figure 14.4, J.M. Butler (2005) Forensic DNA Typing, 2nd Edition © 2005 Elsevier Academic Press







Consumables for ABI 310/3100

What we use at NIST

- A.C.E.™ Sequencing Buffer 10X (Amresco)
  - $155/L = $0.0155/mL 1X buffer (**costs 20 times less!**)
  - http://www.amresco-inc.com
- 3700 **POP-6 Polymer** (Applied Biosystems)
  - $530 / 200 mL = $2.65/mL (**costs 20 times less!**)

What ABI protocols suggest

- 10X Genetic Analyzer Buffer with EDTA
  - $78/25 mL = $0.312/mL 1X buffer (ABI)
- 3100 POP-4 Polymer
  - $365 / 7 mL = $52/mL

2004 prices

Maintenance of ABI 310/3100/3130

- Syringe – leaks cause capillary to not fill properly
- Capillary storage & wash – **it dries, it dies!**
- Pump block – cleaning helps insure good fill
- Change the running buffer regularly

YOU MUST BE CLEAN AROUND A CE!

Overall Thoughts on the ABI 310/3100/3130

- Settling on a common instrument platform has been good for the forensic DNA community in terms of data consistency (this is also true with the use of common STR kits)
- I am concerned that the community is very dependent primarily on one company…
- I really like using the instrument and can usually get nice data from it
- Like any instrument, it has its quirks…

Ways to Increase Sample Throughput

- Run more gels (FMBIO approach)
- Increase speed of single sample analysis (microchip CE systems)
- Multiplex fluorescent dyes of different colors (higher level PCR multiplexes)
- Parallel separations using capillary arrays
- New Detection Technologies (MALDI-TOF mass spectrometry)

Microchip CE Systems

What is under development for STR typing?

What's All the Hype Over Microchip CE Systems?

http://www.washingtonpost.com/wp-dyn/articles/A12570-2003Mar11.html

Attorney General John D. Ashcroft, holding a slide for DNA, hailed the technology as a tool in solving crimes. With him is Kellie Greene, whose attacker was found by DNA testing.

S. Hjertén comments in a 2003 interview

Recently you have been working with chip based techniques. Do you think Lab on a Chip research is a 'fad' or is here to stay?

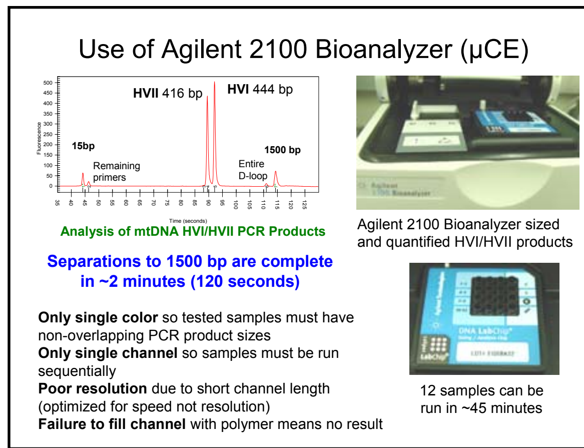
Generally one can state that any method has its advantages and disadvantages: the chip technique is no exception. No doubt, it has its niche, but I think there is some work still to be done. To be used successfully for quantitative analyses one must find simple methods to eliminate adsorption onto the walls of the channels. This is not a simple problem, especially when the sample is protein-based and the chip is made from plastic, the most widely used material. **"Small is beautiful", but not always: when the sample amounts are sufficiently large more robust conventional methods may be preferred.**

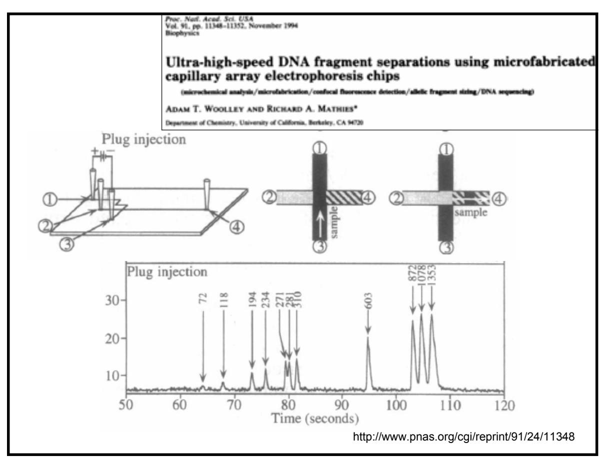
Analyst **(2003) 128: 1307-1309**

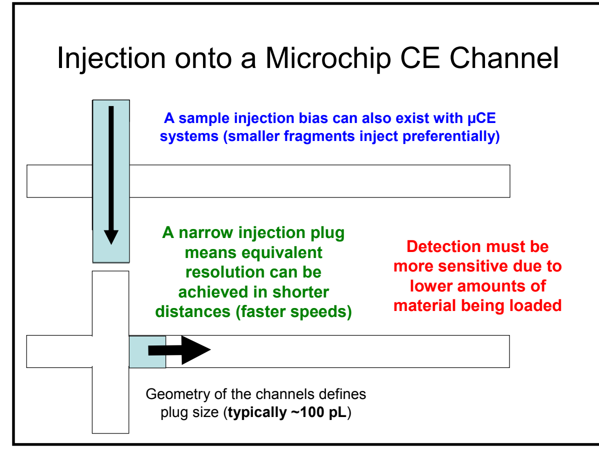
CE Microchips

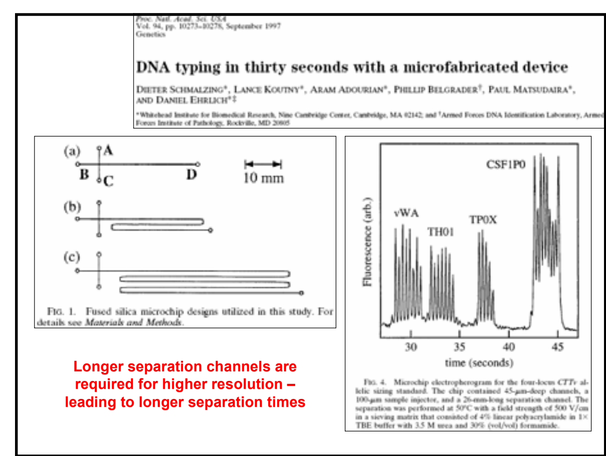
- Channels are etched in glass microscope slides to make miniature CE columns
- More rapid separations are possible due to the shorter separation length (but usually lower resolution)
- Possible to etch many channels CAE microchips

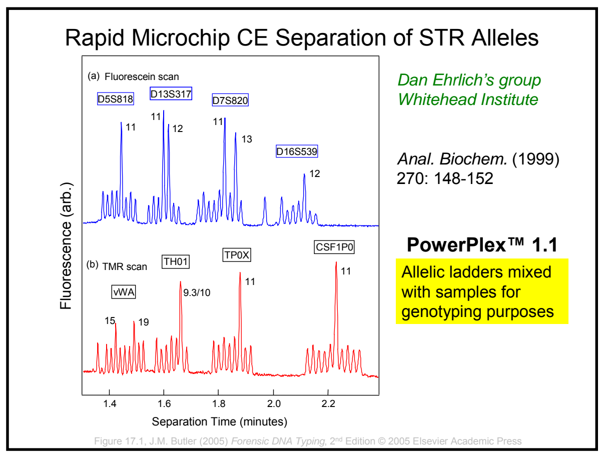
- Sample injection differences with μCE
- Bending channels to get more length slows separation time and introduces possibility of band broadening
- Ratio of injection plug width to separation channel length influences resolution seen

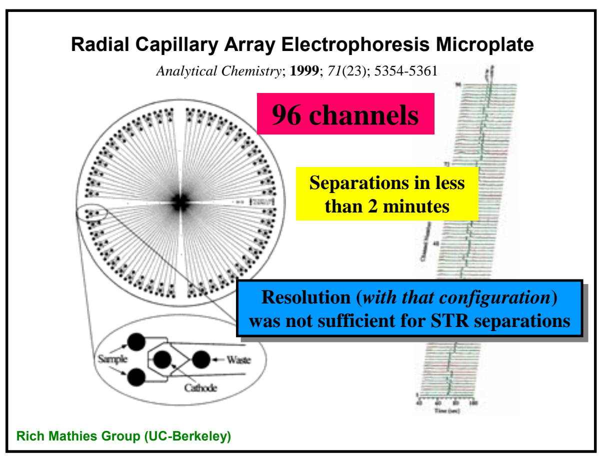


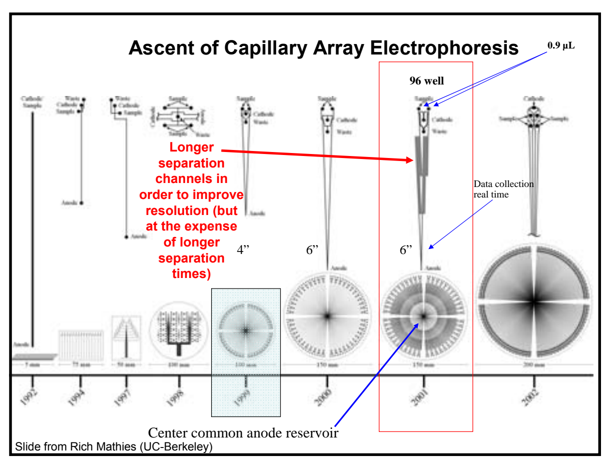


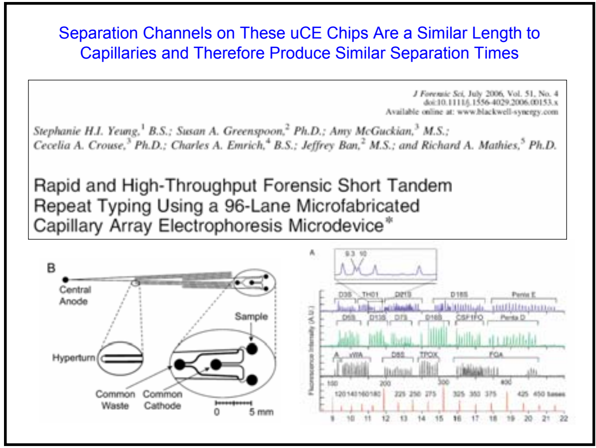


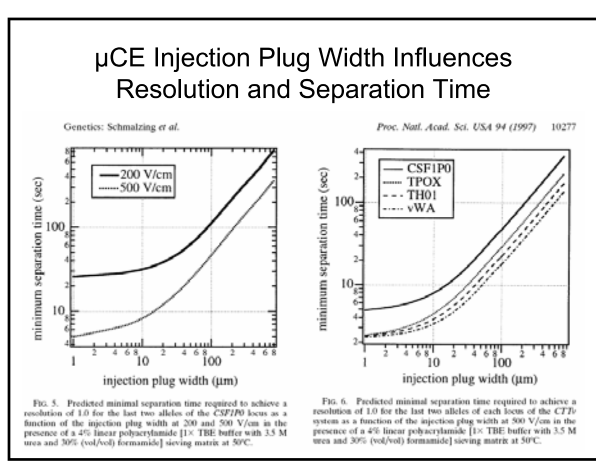


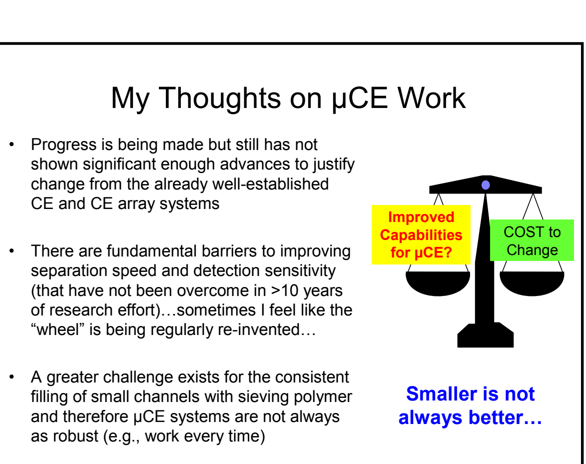

Rapid Microchip CE Separation of STR Alleles
(a) Fluorescein scan
D5S818
D13S317
D7S820
D16S539
(b) TMR scan
TH01
TPOX
CSF1P0
vWA
Fluorescence (arb.)
Separation Time (minutes)
Dan Ehrlich's group
Whitehead Institute
Anal. Biochem. (1999) 270: 148-152
PowerPlex™ 1.1
Allelic ladders mixed with samples for genotyping purposes
Figure 17.1, J.M. Butler (2005) Forensic DNA Typing, 2nd Edition © 2005 Elsevier Academic Press

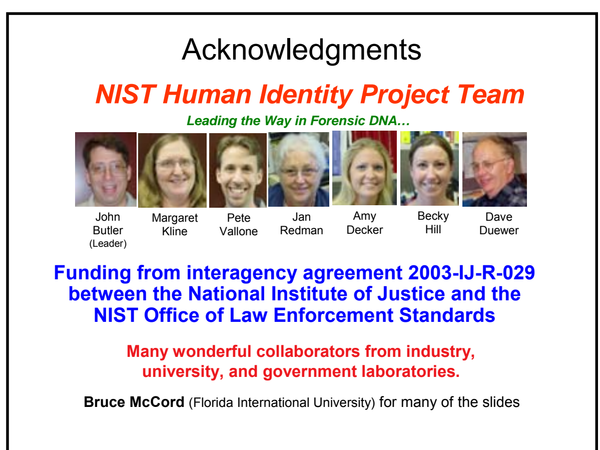

Radial Capillary Array Electrophoresis Microplate
Analytical Chemistry; 1999; 71(23); 5354-5361
96 channels
Separations in less than 2 minutes
Resolution (with that configuration) was not sufficient for STR separations
Sample
Waste
Cathode
Rich Mathies Group (UC-Berkeley)

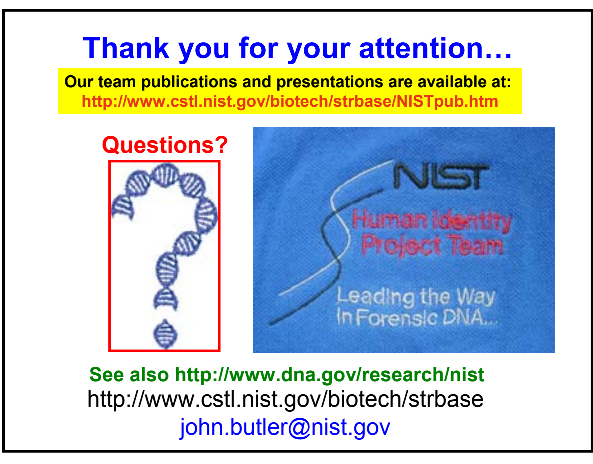

Ascent of Capillary Array Electrophoresis
0.9 µL
96 well
Longer separation channels in order to improve resolution (but at the expense of longer separation times)
Data collection real time
4"
6"
6"
Center common anode reservoir
Slide from Rich Mathies (UC-Berkeley)


Separation Channels on These uCE Chips Are a Similar Length to Capillaries and Therefore Produce Similar Separation Times
J Forensic Sci, July 2006, Vol. 51, No. 4
Stephanie H.I. Yeung, B.S.; Susan A. Greenspoon, Ph.D.; Amy McGuckian, M.S.; Cecelia A. Crouse, Ph.D.; Charles A. Emrich, B.S.; Jeffrey Ban, M.S.; and Richard A. Mathies, Ph.D.
Rapid and High-Throughput Forensic Short Tandem Repeat Typing Using a 96-Lane Microfabricated Capillary Array Electrophoresis Microdevice
Central Anode
Sample
Hyperturn
Common Waste
Common Cathode
5 mm


µCE Injection Plug Width Influences Resolution and Separation Time
Genetics: Schmalzing et al.
Proc. Natl. Acad. Sci. USA 94 (1997) 10277
200 V/cm
500 V/cm
CSF1P0
TPOX
TH01
vWA
minimum separation time (sec)
injection plug width (µm)


My Thoughts on µCE Work
Progress is being made but still has not shown significant enough advances to justify change from the already well-established CE and CE array systems
There are fundamental barriers to improving separation speed and detection sensitivity (that have not been overcome in >10 years of research effort)…sometimes I feel like the "wheel" is being regularly re-invented…
A greater challenge exists for the consistent filling of small channels with sieving polymer and therefore µCE systems are not always as robust (e.g., work every time)
Improved Capabilities for µCE?
COST to Change
Smaller is not always better…


Acknowledgments
NIST Human Identity Project Team
Leading the Way in Forensic DNA…
John Butler (Leader)
Margaret Kline
Pete Vallone
Jan Redman
Amy Decker
Becky Hill
Dave Duewer
Funding from interagency agreement 2003-IJ-R-029 between the National Institute of Justice and the NIST Office of Law Enforcement Standards
Many wonderful collaborators from industry, university, and government laboratories.
Bruce McCord (Florida International University) for many of the slides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Leading the Way in Forensic DNA...
See also http://www.dna.gov/research/nist
http://www.cstl.nist.gov/biotech/strbase
john.butler@nist.gov

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http://www.fsigenetics.com/
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John M. Butler (USA)
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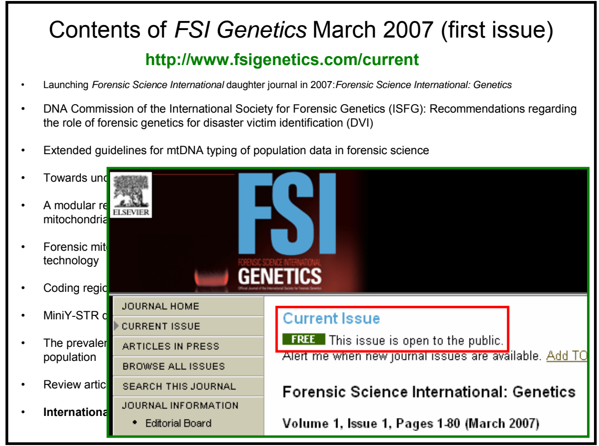
Contents of FSI Genetics March 2007 (first issue)
http://www.fsigenetics.com/current
Launching Forensic Science International daughter journal in 2007: Forensic Science International: Genetics
DNA Commission of the International Society for Forensic Genetics (ISFG): Recommendations regarding the role of forensic genetics for disaster victim identification (DVI)
Extended guidelines for mtDNA typing of population data in forensic science
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Volume 1, Issue 1, Pages 1-80 (March 2007)