

Advanced Topics in Forensic DNA Analysis

Statistics and Population Genetics

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Outline for This Section

- Result interpretation possibilities: exclusion, inconclusive, **match with frequency estimate**
- How allele frequency databases are generated
- Use of the product rule to determine RMP
- OmniPop program

Forensic DNA Typing, 2nd Edition:

Biology, Technology, and Genetics of STR Markers
(John M. Butler, Elsevier Science/Academic Press, 2005)

5 chapters on statistical issues

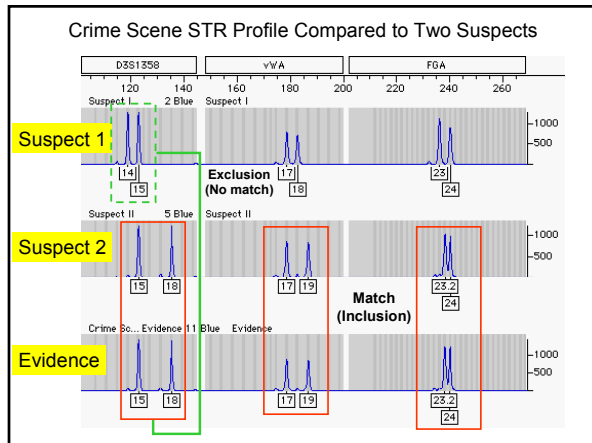
- **Basic Genetic Principles and Statistics**
- **STR Database Analyses**
- **Profile Frequency Estimates**
- **Approaches to Statistical Analysis of Mixtures**
- **Kinship and Paternity Testing**

*Examples are carefully worked through using the same
U.S. population database to illustrate concepts*

Three Possible Outcomes of a DNA Result

Butler, J.M. (2005) *Forensic DNA Typing*, 2nd Edition, p. 385

- **Exclusion (Non-match)** – The genotype comparison shows profile differences that can only be explained by the two samples originating from different sources.
- **Inconclusive** – The data does not support a conclusion as to whether the profiles match. This finding might be reported if two analysts remain in disagreement after review and discussion of the data and it is felt that insufficient information exists to support any conclusion.
- **Match (inclusion)** – Peaks between the compared STR profiles have the same genotypes and no unexplainable differences exist between the samples. Statistical evaluation of the significance of the match is usually reported with the match report.



Single Source Samples

Calculating a Random Match Probability (RMP)

Why Compute a Match Statistic?

- It would not be scientifically justifiable to speak of a match as proof of identity in the absence of underlying data that permit some reasonable estimate of how rare the matching characteristics actually are (NRC II, p. 192).
- Significance or weight of the evidence...

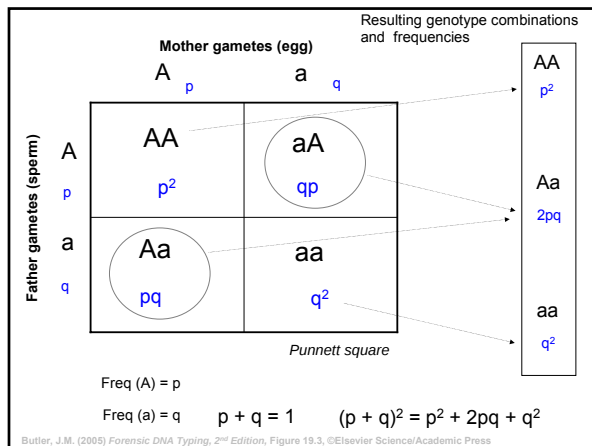
Population Genetics

- Population genetics seeks to understand genetic variation among individuals within and between population groups
- How can we estimate the frequency of a particular DNA profile?
- **Random match probability** - The probability that the DNA in a random sample from the population has the same profile as the DNA in the evidence sample.
([Officers of the Court CD](#))

How Statistical Calculations are Made

- **Generate data** with set(s) of samples from desired population group(s)
 - Generally only 100-150 samples are needed to obtain reliable allele frequency estimates
- **Determine allele frequencies** at each locus
 - Count number of each allele seen
- Allele frequency information is used to **estimate the rarity of a particular DNA profile**
 - **Homozygotes** (p^2), **Heterozygotes** ($2pq$)
 - **Product rule used** (multiply locus frequency estimates)

For more information, see Chapters 20 and 21 in *Forensic DNA Typing, 2nd Edition*



Assumptions behind the Product Rule

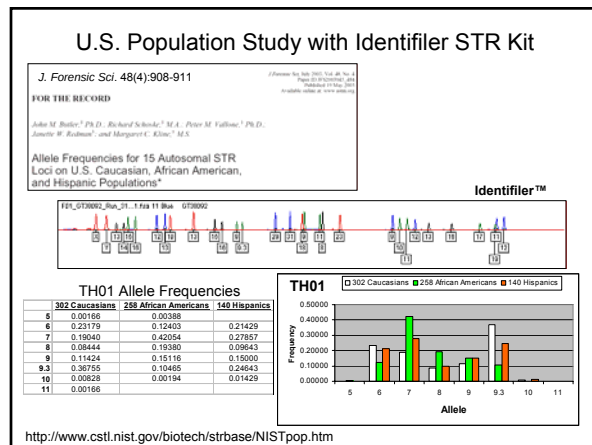
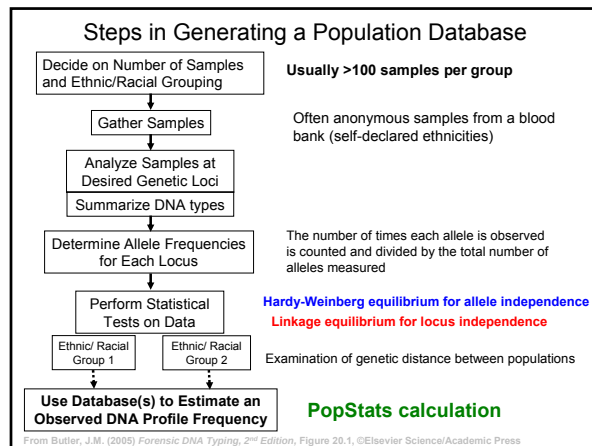
- Independence between alleles (**Hardy-Weinberg equilibrium**)
 - permits correlation of allele frequency with genotype frequency
- Independence between loci (**linkage equilibrium**)
 - permits multiplication of genotype frequencies across all tested loci
- Typically only match probabilities for unrelated individuals are reported

Assumptions with Hardy-Weinberg Equilibrium

The Assumption	The Reason
Large population	Lots of possible allele combinations
No natural selection	No restriction on mating so all alleles have equal chance of becoming part of next generation
No mutation	No new alleles being introduced
No immigration/emigration	No new alleles being introduced or leaving
Random mating	Any allele combination is possible

None of these assumptions are really true...

Butler, J.M. (2005) *Forensic DNA Typing, 2nd Edition*, Table 20.6, ©Elsevier Science/Academic Press



Individual Genotypes Are Summarized and Converted into Allele Frequencies

Genotype Array	8	9	10	11	12	13	14	15	Allele Count	Observed Frequency
8	8,8	8,9	8,10	8,11	8,12	8,13	8,14	8,15	8	0.11258
9		9,9	9,10	9,11	9,12	9,13	9,14	9,15	9	0.07450
10			10,10	10,11	10,12	10,13	10,14	10,15	10	0.05132
11				11,11	11,12	11,13	11,14	11,15	11	0.33940
12					12,12	12,13	12,14	12,15	12	0.24834
13						13,13	13,14	13,15	13	0.12417
14							14,14	14,15	14	0.04801
15								15,15	15	0.00166
									604	

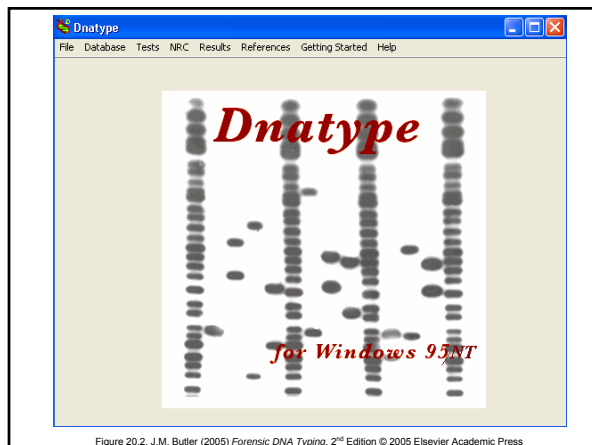
The 11,14 genotype was seen 12 times in 302 samples (604 examined chromosomes)

Butler, J.M. (2005) *Forensic DNA Typing, 2nd Edition*, Table 20.2, ©Elsevier Science/Academic Press

Computer Programs for Performing Statistical Tests on Genetic Data

See Table 20.5 Butler, J.M. (2005) *Forensic DNA Typing, 2nd Edition*

- PowerStats <http://www.promega.com/geneticidtools/default.htm>
- GDA <http://lewis.eeb.uconn.edu/lewishome/software.html>
- GENEPOP <http://wbiomed.curtin.edu.au/genepop/index.html>
- DNA-VIEW <http://www.dna-view.com/> (costs money)
- DNATYPE *Contact Ranajit Chakraborty about availability*
- ARLEQUIN <http://lgb.unige.ch/arlequin/>
- PowerMarker <http://www.powermarker.net>
- PopStats *part of the FBI's CODIS system (not publicly available)*
- TFGPA <http://bioweb.usu.edu/mpmbio/tfpga.asp>



Testing for Independence within a Locus

- Hardy-Weinberg equilibrium (HWE) predicts stability of allele and genotype frequencies from one generation to the next
- Small p values ($p < 0.05$) cast doubt on the validity of the null hypothesis

DNA Statistics

For heterozygous loci

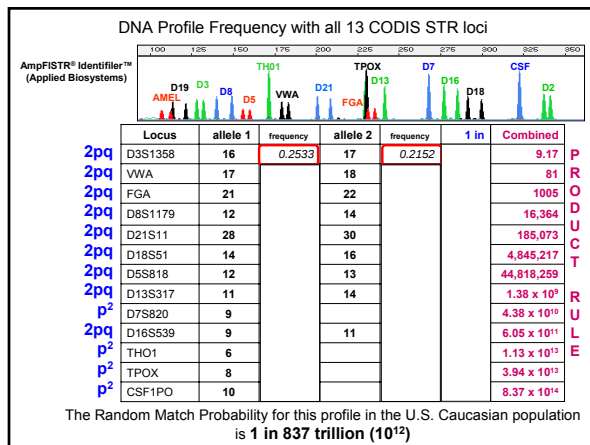
$$P = 2pq$$

P = probability; p and q are frequencies of allele in a given population

Example: For the locus D3S1358 and individual is 16,17 with frequencies of 0.2533 and 0.2152 respectively

$$P = 2(0.2533)(0.2152) = 0.1090 \text{ or } 1 \text{ in } 9.17$$

For independent loci, the genotype frequencies can be combined through multiplication...
Profile Probability = (P1)(P2)...(Pn)
= 1 in a very large number...



Comparison of Results from Different Population Groups

(a)

U.S. Caucasians (N = 302)

DNA Profile		Allele Frequency from Database		Genotype Frequency for Locus	
Locus	Alleles	Times Allele Observed	Size of Database	Frequency	Formula Number
D13S317	11	205	604	$p = 0.34$ $q = 0.05$	$2pq$ 0.03
THO1	6	180	604	$p = 0.23$ $q = 0.14$	p^2 0.05
D18S51	14	83	604	$p = 0.14$ $q = 0.14$	$2pq$ 0.04

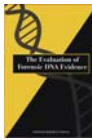
Profile Frequency = 0.000090
 1 in 17,000

(b) U.S. Hispanics (N = 140)

DNA Profile	Allele Frequency from Database				Genotype Frequency for Locus	
Locus	Alleles	Times Allele Observed	Size of Database	Frequency	Formula	Number
D13S317	11	66	280	$p = 0.24$ $q = 0.05$	$2pq$	0.02
THO1	6	60	280	$p = 0.21$ $q = 0.14$	p^2	0.04
D18S51	14	39	280	$p = 0.18$ $q = 0.14$	$2pq$	0.04

Profile Frequency = 0.000032
1 in 31,000

Butler, J.M. (2005) *Forensic DNA Typing, 2nd Edition*, Table 21.1, ©Elsevier Science/Academic Press



NRC II Recommendations for Estimating Random-Match Probabilities

- Recommendation 4.1
 - Use the product rule to calculate profile frequency
 - If perpetrator's race is unknown, report calculations on racial groups for all possible suspects
 - For heterozygotes: use $2p_i p_j$ or $2p_i p_j(1-\theta)$ (eq. 4.4b)
 - For homozygotes: use $p^2 + p(1-p)\theta$ instead of p^2
 - With US population, use $\theta=0.01$
 - With small, isolated populations, use $\theta=0.03$

Why a Theta (θ) Correction?

- Used as a measure of the effects of population subdivision; due to co-ancestry (inbreeding) of alleles
 - Is essentially an attempt to correct for the degree of relatedness of alleles that have a common ancestry
- Basis in fixation indices (F-statistics) described by Sewall Wright in 1951 – F_{ST} , F_{IT} , F_{IS}
 - If the subpopulations are distinct and in HW proportions, then $\theta = F_{ST}$
- Calculations typically performed as described by Weir and Cockerham (1984) Estimating F-statistics for the analysis of population structure. *Evolution* 38: 1358-1370

With US population groups (African Americans, Caucasians, etc.), use $\theta = 0.01$
 With small, isolated populations (Native Americans), use $\theta = 0.03$

Empirical Measurements of Theta (θ)

- Budowle *et al.* (2001) CODIS STR Loci Data from 41 Sample Populations. *J. Forensic Sci.* 46(3): 453-489

TABLE 6— F_{ST} values for the thirteen CODIS core STR loci.

Locus	African American	Caucasian	Hispanic	Asian	Native American
CSF1PO	-0.0009	-0.0007	-0.0003	-0.0012	0.0244
D3S1358	-0.0005	-0.0009	0.0014	0.0035	0.0784
D5S818	0.0010	-0.0001	0.0010	0.0028	0.0656
D7S820	0.0000	-0.0005	0.0010	0.0039	0.0201
D8S1179	-0.0001	0.0000	0.0005	0.0025	0.0125
D18S317	0.0029	-0.0008	0.0047	0.0071	0.0157
D16S539	-0.0013	-0.0005	0.0067	0.0017	0.0132
D18S51	0.0012	0.0001	0.0011	0.0046	0.0268
D21S11	0.0005	0.0008	0.0013	0.0056	0.0371
FGA	0.0004	-0.0004	0.0008	0.0029	0.0168
TH01	0.0015	-0.0012	0.0041	0.0058	0.0356
TPOX	0.0021	-0.0015	0.0024	0.0100	0.0164
vWA	0.0011	-0.0011	0.0029	0.0027	0.0172
F_{ST} over all loci	0.0006	-0.0005	0.0021	0.0039	0.0282

$\theta < 0.01$

$\theta < 0.03$

Empirical Measurements of Theta (θ)

- Budowle and Chakraborty (2001) Population variation at the CODIS core short tandem repeat loci in Europeans. *Legal Med.* 3: 29-33
- "Because of the low value for theta, whether independence is assumed or an adjustment for substructure is employed, **there is little practical consequence for forensic purposes for estimating the frequency of a multiple locus DNA profile.** If theta is used, a value of 0.01 is very conservative for Europeans."
- **F_{ST} over all loci = 0.0028**

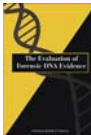
Basis of PopStats Calculations

Budowle et al. (2001) *J. Forensic Sci.* 46(3): 453-489

Bruce Budowle,¹ Ph.D.; Brendan Shea,² M.S.; Stephen Niezgoda,² M.B.A.; and Ranajit Chakraborty,³ Ph.D.

CODIS STR Loci Data from 41 Sample Populations* **Data collected by 20 different forensic laboratories**

The F_{ST} estimates over all thirteen STR loci are
 0.0006 for African Americans,
 -0.0005 for Caucasians,
 0.0021 for Hispanics,
 0.0039 for Asians,
 and 0.0282 for Native Americans.



NRC II Recommendations for Estimating Random-Match Probabilities When Sub-Group Data Are Not Available

Recommendation 4.2. If the particular subpopulation from which the evidence sample came is known, the allele frequencies for the specific subgroup should be used as described in Recommendation 4.1. If allele frequencies for the subgroup are not available, although data for the full population are, then the calculations should use the population-structure equations 4.10 for each locus, and the resulting values should then be multiplied.

$$\text{Homozygote: } P(A_i A_i | A_i A_i) = \frac{[2\theta + (1 - \theta)p_i][3\theta + (1 - \theta)p_i]}{(1 + \theta)(1 + 2\theta)} \quad (4.10a)$$

$$\text{Heterozygote: } P(A_i A_j | A_i A_j) = \frac{2[\theta + (1 - \theta)p_i][\theta + (1 - \theta)p_j]}{(1 + \theta)(1 + 2\theta)} \quad (4.10b)$$

Butler, J.M. (2005) Forensic DNA Typing: Biology, Technology, and Genetics of STR Markers, 2nd Edition, Elsevier: New York: Appendix VI, pp. 623-625

Comparison of Results Obtained with Various NRC II Formula

Under HWE		Unconditional (NRCII Recommendation 4.1)	Conditional with Substructure Adjustment
		(NRCII recommendation 4.10a)	
Homozygote	p^2	$p^2 + p(1-p)\theta$	$\frac{[p(1-\theta) + 2\theta][p(1-\theta) + 2\theta]}{(1+\theta)(1+2\theta)}$
TH01 6,6	(0.23) ² = 0.053 $\theta = 0.01$	(0.23) ² + (0.23)(1-0.23)(0.01) = 0.053 + 0.0018 = 0.055 1 in 18.9	$\frac{[(0.23(1-0.01) + 2(0.01)][(0.23(1-0.01) + 2(0.01))]}{(1+0.01)(1+2(0.01))}$ = (0.2477)(0.2577)/(1.01)(1.02) = 0.062 1 in 16.1
		(NRCII recommendation 4.10b)	
Heterozygote	$2p_i p_j$	$2p_i p_j(1-\theta)$ eq. (4.4b); NRCII, p. 102	$\frac{2[p_i(1-\theta) + 2\theta][p_j(1-\theta) + 2\theta]}{(1+\theta)(1+2\theta)}$
D15S11 11,14	2(0.34)(0.05) = 0.0340 $p_i = 0.34$ $p_j = 0.05$ $\theta = 0.01$	2(0.34)(0.05)(1-0.01) = 0.0337 1 in 29.4	$\frac{2[(0.34(1-0.01) + 2(0.01)][(0.05(1-0.01) + 2(0.01))]}{(1+0.01)(1+2(0.01))}$ = 2(0.3466)(0.0595)/(1.01)(1.02) = 0.0400 1 in 25.0

Butler, J.M. (2005) *Forensic DNA Typing, 2nd Edition*, Table 21.4, ©Elsevier Science/Academic Press

Example Calculations with Population Substructure Adjustments

Table 21.5
Example calculations with NRC II recommendations for population substructure adjustments (see Appendix VI). Scenarios with data equal to 0.01 and 0.03 are omitted.

From U.S. Caucasian (N=302): Appendix II - sample in database				Under HWE		NRCII recommendation 4.1		NRCII recommendation 4.10	
A1	A2	A1 Allele 1 freq (q)	A2 Allele 2 freq (q)	Calc freq		$\theta = 0.01$	$\theta = 0.03$	$\theta = 0.01$	$\theta = 0.03$
D15S11	11 14	0.33948	0.04801	2pq	0.0326	0.0326	0.0326	eq. 4.10a	0.0386
TH01	6 6	0.23179	—	p^2	0.0537	$p^2 + p(1-p)\theta$	0.0555	eq. 4.10a	0.0628
D16S51	14 16	0.13742	0.12907	2pq	0.0382	0.0382	0.0382	eq. 4.10a	0.0419
D21S11	28 30	0.15894	0.27815	2pq	0.0684	0.0684	0.0684	eq. 4.10a	0.0927
D3S1358	16 17	0.25331	0.21523	2pq	0.1090	0.1090	0.1090	eq. 4.10a	0.1129
D5S818	12 13	0.38411	0.14073	2pq	0.1081	0.1081	0.1081	eq. 4.10a	0.1131
D7S820	9 9	0.17715	—	p^2	0.0314	$p^2 + p(1-p)\theta$	0.0328	eq. 4.10a	0.0390
D8S1179	12 14	0.18543	0.16556	2pq	0.0614	0.0614	0.0614	eq. 4.10a	0.0654
CFR1PO	10 10	0.21683	—	p^2	0.0470	$p^2 + p(1-p)\theta$	0.0487	eq. 4.10a	0.0558
FGA	21 22	0.18543	0.21854	2pq	0.0810	0.0810	0.0810	eq. 4.10a	0.0851
D16S539	9 11	0.11258	0.32119	2pq	0.0723	0.0723	0.0723	eq. 4.10a	0.0773
TPOX	8 8	0.53477	—	p^2	0.2860	$p^2 + p(1-p)\theta$	0.2885	eq. 4.10a	0.2983
VWA	17 18	0.28146	0.20033	2pq	0.1128	0.1128	0.1128	eq. 4.10a	0.1187
AMEL	X Y	—	—	—	—	—	—	—	—

Butler, J.M. (2005) *Forensic DNA Typing, 2nd Edition*, Table 21.5, ©Elsevier Science/Academic Press

NRC II Recommendations for Estimating Random-Match Probabilities

- Recommendation 4.3.** If the person who contributed the evidence sample is from a group or tribe for which no adequate database exists, **data from several other groups or tribes thought to be closely related to it should be used.** The profile frequency should be calculated as described in Recommendation 4.1 for each group or tribe.

- For heterozygotes: use $2p_i p_j$
- For homozygotes: use $p^2 + p(1-p)\theta$ instead of p^2

Allele frequencies denoted with an asterisk (*) are below the 5/2N minimum allele threshold recommended by the National Research Council report (NRCII) *The Evaluation of Forensic DNA Evidence* published in 1996.

Butler et al. (2003)
JES 48(4):908-911Einum et al. (2004)
JES 49(6)

Caucasian

N= 302

Caucasian

N= 7,636

**African
American**

N=258

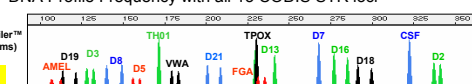
**African
American**

N= 7,602

>25X
number
of
samples

	N=302		N=7,636		N=256		N=7,602	
	Allele				Allele			
Most common allele	11	0.0017*	0.0009		11	--	0.0003*	
	12	0.0017*	0.0007		12	--	0.0045	
	13	--	0.0031		13	0.0019*	0.0077	
	14	0.1027	0.1240		14	0.0892	0.0905	
	15	0.2616	0.2690		15	0.3023	0.2920	
	15.2	--	--		15.2	0.0019*	0.0010	
	16	0.2533	0.2430		16	0.3353	0.3300	
	17	0.2152	0.2000		17	0.2054	0.2070	
	18	0.15232	0.1460		18	0.0601	0.0630	
	19	0.01160	0.0125		19	0.0039*	0.0048	
20	0.0017*	0.0001*		20				

AmpFISTR® Identifiler™
(Applied Biosystems)



What would be entered into a DNA database for searching:

Locus	allele	frequency	allele	frequency	1 in	Combined
D3S1358	16	0.2533	17	0.2152	9.17	9.17
VWA	17	0.2815	18	0.2003	8.87	81
FGA	21	0.1854	22	0.2185	12.35	1005
D8S1179	12	0.1854	14	0.1656	16.29	16,364
D21S11	28	0.1589	30	0.2782	11.31	185,073
D18S51	14	0.1374	16	0.1391	26.18	4,845,217
D5S818	12	0.3841	13	0.1407	9.25	44,818,259
D13S317	11	0.3394	14	0.0480	30.69	1.38×10^3
D7S820	9	0.1772			31.85	4.38×10^{10}
D16S539	9	0.1126	11	0.3212	13.8	6.05×10^{11}
THO1	6	0.2318			18.62	1.13×10^{13}
TPO	8	0.5348			3.50	3.94×10^{13}
CSF1PX	10	0.2169			21.28	8.37×10^{14}

The Random Match Probability for this profile in the U.S. Caucasian population is **1 in 837 trillion (10^{12})**

1 in 837 trillion

1 in 0.84 quadrillion (10^{15}) in U.S. Caucasian population (NIST)

1 in 2.46 quadrillion (10^{15}) in U.S. Caucasian population (FBI)*

1 in 1.86 quadrillion (10^{15}) in Canadian Caucasian population*

1 in 16.6 quadrillion (10^{15}) in African American population (NIST)

1 in 17.6 quadrillion (10¹⁵) in African American population (FBI)*

1 in 18.0 quadrillion (10^{15}) in U.S. Hispanic population (NIST)

These values are **for unrelated individuals**
assuming no population substructure (using only p^2 and $2pq$)

NIST study: Butler, J.M., et al. (2003) Allele frequencies for 15 autosomal STR loci on U.S. Caucasian, African American, and Hispanic populations. *J. Forensic Sci.* 48(4):908-911. (<http://www.cstl.nist.gov/biotech/strbase/NISTpop.htm>)

*<http://www.csfs.ca/pplus/profiler.htm>

Theoretical **Most** Common STR Type

Locus	A1	A2	Allele 1 Freq (q)	Allele 2 Freq (q)	Most Common Genotype Frequency
D13S317	11	12	0.33940	0.24834	2pq 0.1686
D16S939	12	11	0.32816	0.32119	2pq 0.2095
D18S51	15	16	0.15894	0.13907	2pq 0.0442
D21S11	30	29	0.27815	0.19536	2pq 0.1087
D5S1358	15	16	0.26199	0.25331	2pq 0.1325
DV0018	12	11	0.36811	0.36093	2pq 0.2773
D7S200	10	11	0.24330	0.26095	2pq 0.1007
D8S1179	13	12	0.30854	0.18543	2pq 0.1130
CSF1PO	12	11	0.36099	0.30132	2pq 0.2175
FGA	22	21	0.21854	0.18543	2pq 0.0810
TH01	9.3	8	0.36255	0.23179	2pq 0.1704
TP0X	8	11	0.53477	0.24038	2pq 0.2493
VWA	17	18	0.28146	0.20033	2pq 0.1128

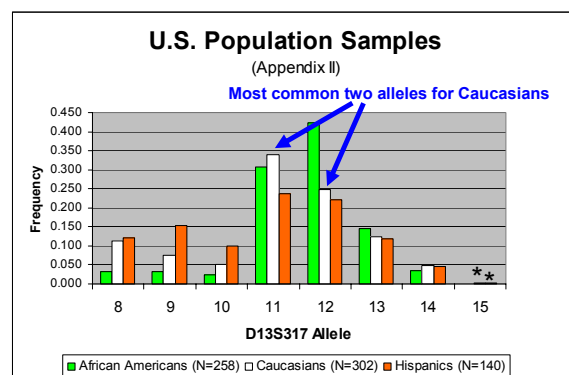
Calculations for the theoretically most common genotype frequencies and profile frequency based on two most common alleles found in a U.S. Caucasian allele frequency database

6.26×10^{-12}
or 1 in 160 billion

1 in... 1.60×10^{11} (160 billion)

Butler, J.M. (2005) *Forensic DNA Typing, 2nd Edition*, Table 20.9, ©Elsevier Science/Academic Press

Figure 20.3



Butler, J.M. (2005) *Forensic DNA Typing, 2nd Edition*, Figure 20.3, ©Elsevier Science/Academic Press

Theoretical **Least** Common STR Type

Using $5/2N$ minimum allele frequency rule

If $N = 302$, then $5/2N = 0.00828 = p = q$

And $(2pq)^{13} = [2 \times 0.00828 \times 0.00828]^{13}$

6.06×10^{-51}
or 1 in 1.65×10^{50}

Websites for Software Used in Match Probability Calculations

- **OmniPop** (<http://www.cstl.nist.gov/biotech/strbase/populationdata.htm>)
 - is an Excel-based program developed by a forensic scientist named Brian Burritt of the San Diego Police Department. OmniPop calculates a user-inputted STR profile's frequency using allele frequencies from 202 published databases. The program is freely available for download from the NIST STRBase website.
- **European Network of Forensic Science Institutes DNA Working Group STR Population Database** (<http://www.str-base.org/index.php>)
 - uses 5,699 samples from 24 European populations in order to make match probability calculation on user-inputted STR profiles containing the 10 STR loci present in the SGM Plus kit (Applied Biosystems) that is widely used in Europe.
- **Canadian Random Match Calculator** (<http://www.csfs.ca/pplus/profiler.htm>)
 - enables calculation of user-inputted STR profiles for the 13 U.S. core STR loci amplified by the Profiler Plus and Cofiler kits sold by Applied Biosystems. This program enables comparison of results from limited FBI and Canadian collected allele frequencies.

OmniPop Program

Available from <http://www.cstl.nist.gov/biotech/strbase/populationdata.htm>

Due to the fact that DNA typing is only an examination of a DNA sample's sequence and/or length at discrete locations, a match in DNA typing is always a statistical exercise. (Currently, time and expense limit an examination of an individual's entire genome, which would show unique identity for all but identical twins.) In order to determine the probability that a particular genotype might occur at random in a population, population data must be gathered to make an estimate of the frequency of each possible allele and genotype. Usually a sample size of greater than 100 samples is sufficient to make reliable projections about a genotype's frequency in a larger population (see Chakraborty, R. (1992) *Human Biology* 64:141-159).

The data collected and presented here represent information from published sources (see [reference listing](#)). The population sampled is listed by its reference number according to the commercial kit used to collect the data. We hope this information will be helpful to the DNA typing community for comparing results between populations.

[Population Survey](#) provided by [Brian Burritt \(San Diego Police Department\)](#) **Updated**

[Reference Listing](#) of Published Sources (**212 publications** as of 12/01/2006)

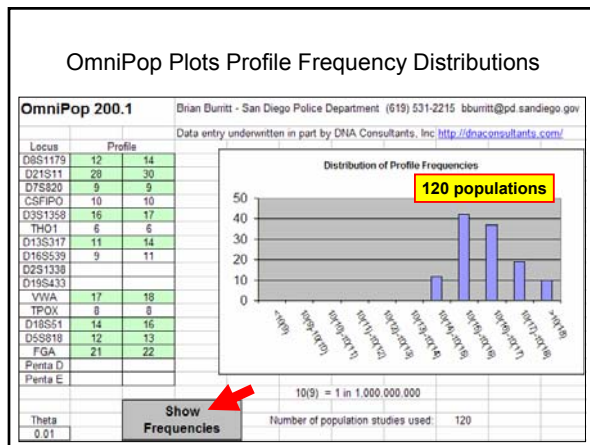
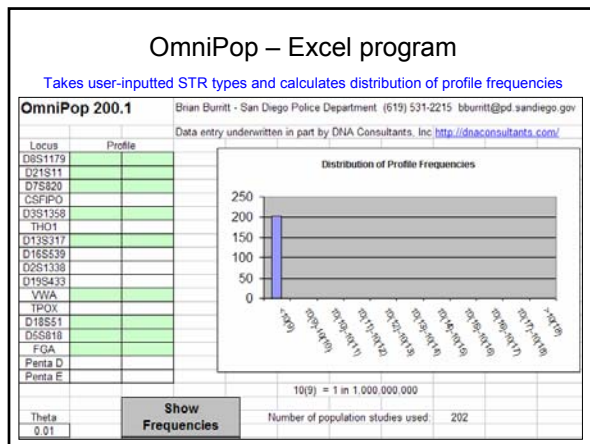
[Download OmniPop program](#) (~1.7 Mbytes macro-enabled Excel file developed by [Brian Burritt](#)) **Updated**

- OmniPop calculates a user-inputted profile's frequency using allele frequencies from **202** published databases present in the program (*updates will be made available in the future*)

<http://www.cstl.nist.gov/biotech/strbase/population/OmniPop200.1.xls>

OmniPop 200.1

- **Published allele frequencies**
 - From 120 populations containing all 13 CODIS loci
 - From 202 populations with 9 loci (Profiler Plus)
- **Based on 89 publications**
- **Available from Brian Burritt (San Diego Police Dept)**
 - (619) 531-2215
 - bburritt@pd.sandiego.gov



OmniPop Lists Frequency Calculations for All 120 Populations

Most Common Profile Frequencies		Least Common Profile Frequencies	
Serbian (157)	1.42E+14	Athabaskan (Alaska) (60)	9.65E+18
Portuguese (6)	3.43E+14	Inupiat (Alaska) (60)	1.71E+20
Belgian (99)	6.76E+14	Yupik (Alaska) (60)	2.02E+20
Caucasian (64)	7.43E+14	PC/BT-Asian (4)	3.77E+20
Swiss Caucasian (3)	7.59E+14	Canadian Aboriginal (56)	6.54E+20
Azores (82)	7.68E+14	Navajo (2)	7.09E+20
Scottish (11)	7.89E+14	Apache (2)	2.65E+21

OmniPop References

2 - CODIS STR Loci Data from 41 Sample Populations, J Forensic Sci, 2001, 46(3), 453-489.

60 - Population studies on three Native Alaska population groups using STR loci, FSI, 2002, p51-57

64 - Allele Frequencies for 15 Autosomal STR Loci in U.S. Caucasian, African American, and Hispanic Populations, JFS, 2003, p908-911

157 - Allele frequencies of the 15 AmpFISTR Identifier loci in the population of Vojvodina Province, Serbia and Montenegro, JLM, 2004, 184-186

STR Cumulative Profile Frequency with Multiple Population Databases				
STR Locus	Profile Computed	Number of Populations Used	Cumulative Profile Frequency Range (1 in ...)	Cumulative Profile Frequency against U.S. Caucasians (Appendix II)
D3S1358	16,17	166	5.24 to 62.6	9.19
VWA	17,18	166	37.6 to 1080	81.8
FGA	21,22	166	737 to 119,000	1010
D8S1179	12,14	166	8980 to 5,430,000	16,400
D21S11	28,30	166	165,000 to 248,000,000	186,000
D18S51	14,16	166	3.85×10^4 to 2.68×10^6	4.88×10^6
D5S818	12,13	166	2.28×10^4 to 4.22×10^{11}	4.51×10^7
D13S17	11,14	166	4.32×10^4 to 1.69×10^{13}	1.38×10^9
D7S820	9,9	166	1.17×10^{10} to 2.98×10^{16}	4.22×10^{10}
D16S539	9,11	97	4.06×10^{11} to 1.11×10^{18}	5.82×10^{11}
TH01	6,6	97	9.30×10^{12} to 1.45×10^{19}	1.05×10^{12}
TPOX	8,8	97	3.33×10^{11} to 1.54×10^{18}	3.63×10^{11}
CSF1PO	10,10	97	3.43×10^{14} to 2.65×10^{21}	7.43×10^{14}

Butler, J.M. (2005) *Forensic DNA Typing*, 2nd Edition, D.N.A. Box 21.1, ©Elsevier Science/Academic Press

Theoretical RMP Range

 6.26×10^{-12}
 or 1 in 160 billion

 6.06×10^{-51}
 or 1 in 1.65×10^{50}

Observed RMP Range

 10^{14} to 10^{21}

DNA Advisory Board Statistics Article

Discusses

- Source attribution or identity
- Cases where relatives may be involved
- Interpretation of mixtures
- Significance of a match derived through a DNA database search

**FORENSIC SCIENCE
COMMUNICATIONS**
 July 2000 Volume 2 Number 3

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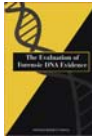
JOURNAL

Statistical and Population Genetics
Issues Affecting the Evaluation of
the Frequency of Occurrence of
DNA Profiles Calculated From
Pertinent Population Database(s)

 DNA Advisory Board
 February 23, 2000

<http://www.fbi.gov/hq/lab/fsc/backissu/july2000/dnastat.htm>

Impact of Relatedness on Match Probabilities



NRC II Recommendations for Estimating Random-Match Probabilities When Relatives May Be Involved

Recommendation 4.4. If the possible contributors of the evidence sample include relatives of the suspect, DNA profiles of those relatives should be obtained. If these profiles cannot be obtained, the probability of finding the evidence profile in those relatives should be calculated with Formulae 4.8 or 4.9.

Genotype of suspect Probability of same genotype in a relative

$$\text{Homozygote: } A_1A_1 \quad p_1^2 + 4p_1(1-p_1)F \quad (4.8a)$$

$$\text{Heterozygote: } A_1A_2 \quad 2p_1p_2 + 2(p_1 + p_2 - 4p_1p_2)F \quad (4.8b)$$

For parent and offspring, $F = 1/4$; for half-siblings, $1/8$; for uncle and nephew, $1/8$; for first cousins, $1/16$.

Full siblings, being bilinear rather than unilinear, require different formulae:

$$A_1A_1: (1 + 2p_1 + p_1^2)/4 \quad (4.9a)$$

$$A_1A_2: (1 + p_1 + p_2 + 2p_1p_2)/4 \quad (4.9b)$$

Butler, J.M. (2005) *Forensic DNA Typing: Biology, Technology, and Genetics of STR Markers*, 2nd Edition, Elsevier: New York: Appendix VI, pp.623-625

Example Calculations with Corrections for Relatives

Table 21.6

Example calculations with corrections for relatives using the NRC II recommended formula.

From U.S. Caucasian (N = 302): Appendix B - sample in database (color 100)						NRC II Recommendation 4.4			
A1	A2	Allele 1 freq (q)	Allele 2 freq (p)	Calc. freq		F = 1/4 (parent)	F = 1/8 (half sib)	F = 1/16 (1st cousin)	Full sib
D1S317	11 14	0.33940	0.04801	2pq	0.8326	eq. 4.8a 0.1937	0.1131	0.0729	eq. 4.9b 0.3550
TH01	6 8	0.23179	—	p ²	0.0537	eq. 4.8a 0.2318	0.1428	0.0982	eq. 4.9a 0.3793
D16S39	9 11	0.13258	0.32119	2pq	0.0723	eq. 4.8b 0.2469	0.1446	0.1085	eq. 4.9b 0.3755
D18S51	14 16	0.13742	0.13907	2pq	0.0382	eq. 4.8b 0.1362	0.0982	0.0632	eq. 4.9b 0.3287
D21S11	28 30	0.15094	0.27815	2pq	0.0894	eq. 4.8b 0.2185	0.1535	0.1209	eq. 4.9b 0.3814
D3S1358	16 17	0.25331	0.21523	2pq	0.1090	eq. 4.8b 0.2343	0.1717	0.1403	eq. 4.9b 0.3944
D5S818	12 13	0.38411	0.14073	2pq	0.1081	eq. 4.8b 0.2624	0.1853	0.1467	eq. 4.9b 0.4082
D7S820	9 9	0.17715	—	p ²	0.0314	eq. 4.8a 0.1772	0.1043	0.0678	eq. 4.9a 0.3464
D8S1179	12 14	0.18543	0.16556	2pq	0.0614	eq. 4.8b 0.1795	0.1184	0.0889	eq. 4.9b 0.3531
CFP190	10 10	0.21689	—	p ²	0.0470	eq. 4.8a 0.2169	0.1330	0.0895	eq. 4.9a 0.3792
FGA	21 22	0.18543	0.21854	2pq	0.0810	eq. 4.8b 0.2020	0.1415	0.1113	eq. 4.9b 0.3713
TPOX	8 8	0.53477	—	p ²	0.2860	eq. 4.8a 0.5348	0.4104	0.3482	eq. 4.9a 0.5889
VR1A	17 18	0.28146	0.20033	2pq	0.1128	eq. 4.8b 0.2409	0.1768	0.1468	eq. 4.9b 0.3905
AMEL	X Y								
					1.20E-15	3.17E-09	1.88E-11	3.74E-13	4.08E-06 1 in 247,516

Effects of Family Relatedness on Match Probabilities

Relationship	Match probability formula	Result with TH01 6,8	p = 0.23179
Homozygotes (A ₁ A ₁)			
Full siblings	$\frac{(1+p_1^2 + (1-p_1)^2 - 2p_1(1-p_1) + (1-p_1)^2 - 2p_1(1-p_1))}{4(1+p_1(1-p_1))}$	0.38921	
Parent and child	$\frac{2p_1(1-p_1)}{(1+p_1)}$	0.24700	
Half siblings	$\frac{2p_1(1-p_1)(2+4p_1(1-p_1))}{2(1+p_1(1-p_1))}$	0.27479	
First cousins	$\frac{2p_1(1-p_1)(2+10p_1(1-p_1))}{4(1+p_1(1-p_1))}$	0.10888	
Unrelated	$\frac{2p_1(1-p_1)(1+p_1(1-p_1))}{4(1+p_1(1-p_1))}$	0.06283	
(NRC II, 4.10a)			
Heterozygotes (A ₁ A ₂)			
Full siblings	$\frac{(1+p_1+p_2+2p_1p_2+(1-p_1)^2-4p_1p_2+2(1-p_1)^2-2p_1(1-p_1))}{4(1+p_1(1-p_1))}$	0.35955	
Parent and child	$\frac{2p_1(1-p_1)p_2}{2(1+p_1)}$	0.19977	
Half siblings	$\frac{(p_1+p_2+4p_1p_2+(2+5p_1+5p_2+10p_1p_2)+2(1-p_1)^2-4p_1p_2+2(1-p_1)^2-2p_1(1-p_1))}{4(1+p_1(1-p_1))}$	0.11921	
First cousins	$\frac{(p_1+p_2+12p_1p_2+(2+13p_1+13p_2+24p_1p_2)+2(1-p_1)^2-4p_1p_2+2(1-p_1)^2-2p_1(1-p_1))}{8(1+p_1(1-p_1))}$	0.07893	
Unrelated	$\frac{2p_1(1-p_1)p_2}{2(1+p_1(1-p_1))}$	0.03864	
(NRC II, 4.10b)			
		2pq = 0.03259	p = 0.33940 q = 0.04801

Butler, J.M. (2005) *Forensic DNA Typing*, 2nd Edition, Table 21.7, ©Elsevier Science/Academic Press

Obtain DNA from All Possible Suspects

- As expressed by NRC II Recommendation 4.4, "if possible contributors of the evidence sample include relatives of the suspect, **DNA profiles of those relatives should be obtained.**"
- In other words, avoid the hypothetical and test the related individual in order to see if a direct match occurs between the evidence and the suspect...

Mixture Statistics

Approaches to Mixture Analysis and Statistics

Ladd *et al.* (2001) *Croatian Med. J.* 42(3): 244-246

- Qualitative Assessment (inclusion or exclusion of suspect)
- Deduction of Component Profiles followed by Calculation of Match Probabilities
- Probability of Exclusion (or Inclusion)
- Likelihood Ratio

ISFG Recommendations on Mixture Interpretation

July 13, 2006 issue of *Forensic Science International*Available online at www.sciencedirect.com

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Forensic Science International 160 (2006) 90–108

www.elsevier.com/locate/forensiDNA commission of the International Society of Forensic Genetics:
Recommendations on the interpretation of mixturesP. Gill^{a,*}, C.H. Brenner^b, J.S. Buckleton^c, A. Carracedo^d, M. Krawczak^e, W.R. Mayr^f,
N. Morling^g, M. Prinz^h, P.M. Schneiderⁱ, B.S. Weir^j^aForensic Science Service, Trident Court, 2000 Solihull Parkway, Birmingham, UK^bForensic Science Group, School of Public Health, University of California Berkeley, CA 94720-7411, USA^cESR, Private Bag 92021, Auckland, New Zealand^dInstitute of Legal Medicine, Faculty of Medicine, University of Santiago de Compostela, 15705 Santiago de Compostela, Spain^eInstitute of Medical Informatics and Statistics, Kiel, Germany^fDivision of Blood Group Serology, Medical University of Vienna, Austria^gDepartment of Forensic Genetics, Institute of Forensic Medicine, University of Copenhagen, Copenhagen, Denmark^hOffice of the Chief Medical Examiner, Department of Forensic Biology, 520 First Avenue, New York, NY 10036, USAⁱInstitute of Legal Medicine University Clinic of Cologne, Melanienstrasse, 50692 D-50692 Köln, Germany^jUniversity of Washington, Department of Biostatistics, Box 357232, Seattle, WA 98195, USA

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**Discuss probability of exclusion
and likelihood ratio methods**

Statistical Calculations for Lineage Markers

Y-Chromosome and Mitochondrial DNA

Counting Method Typically Used for Lineage Markers

- Number of times that a particular DNA type occurs in a population database (frequency point estimate)
- Sampling corrections can be made with 95% confidence interval around the frequency point estimate