A Guide to
Forensic DNA Profiling

Editors-in-Chief

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WILEY

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Foreword

My contact with Professor Jamieson and Dr Bader (or Allan and Scott as I now know them and shall refer to them) began in the seminal trial of Sean Hoey (in relation to the Omagh Bombing) in Northern Ireland in 2007. This was the firs serious challenge in the United Kingdom to the use of low copy number (LCN) DNA profiling the first form of what has become more generally known as low template DNA profiling Although Mr Hoey was primarily acquitted as a result of reservations surrounding the way in which key exhibits were seized, stored, and examined, the learned trial judge, the Honorable Mr Justice Weir, raised concerns in relation to the reliability of interpreting LCN DNA. Such concerns were no doubt borne out of the points we advanced on behalf of Mr Hoey, which were in turn borne out of the concerns of those from The Forensic Institute. From the outset, The Forensic Institute expressed the strongest of reservations as to the reliability of interpreting such minute amounts of DNA found on the relevant exhibits (none of which were from the Omagh incident as it happens).

These concerns caused a seismic response in scientifi and legal circles, which continues to this day. Toward the end of 2014, I had the pleasure of working with Allan and Scott in a murder trial at the Old Bailey. They were instructed on behalf of the defense to comment upon the reliability and inter-pretability of low template DNA recovered from a murder scene. In this recent case, part of the argument focused upon the reliability of the methods employed by the prosecution to quantify the probative value of such low amounts of DNA. One of the methods employed involved the use of software, which was said to overcome the complex nature of the results; another was the "counting method." Following the cross-examination of one of the prosecution's lead forensic scientists the Crown withdrew the DNA evidence in the case.

There is no doubt that for lawyers, DNA profilin can present a daunting challenge. This is not only in understanding the science involved, but also in knowing how best to present the results in a way that can be easily understood. I am indebted to Allan and Scott for guiding our legal teams through the morass of graphs, statistics, and terminology, enabling us to be able to properly represent our clients on the most serious of allegations. I am optimistic that the clarity of their approach and the appreciation of the needs of the non-specialist will be reflecte in the content of this book.

I am also delighted to learn that this will be one of the few books that brings together the scientifi and legal aspects of DNA profilin in such a comprehensive approach. That is not an easy task; but I know that the Editors had assistance from Professor Andre Moenssens of the *Wiley Encyclopedia of Forensic Science* where many of the articles in this book originate.

Needless to say I write this having not read all of the articles in this work, but I am confiden that if the skills I have taken advantage of in our casework are taken into the production of this work then it will provide a valuable resource for both lawyers and experts alike in the continuing quest to tackle the increasingly complex issues involved in forensic DNA profiling

A lawyer writing a preface for a book written by scientists? Progress indeed.

Kieran Vaughan QC
Garden Court Chambers

Preface

Forensic DNA profilin has revolutionized forensic science. However, from relatively simple beginnings using what would now be regarded as huge amounts of sample (e.g., bloodstain), not only has the underlying technology changed (i.e., RFLP to STRs and SNPs) but the complexity of the interpretation of the analytical results has increased in the quest to get more information from smaller, and more complex, samples.

Most of these developments are published and debated in the scientifi literature, although some are guarded for ostensibly commercial reasons, or sometimes it seems simply to avoid showing one's hand to the other side in an adversarial legal system. Much of the scientifi and statistical debate remains active and there is no settled position. Indeed, it could be contended that in many of these arguments each side has a rational and reasoned position, simply different to their opponents.

This book does not seek to provide or claim to have the final answer on any of these, because for many issues there is none. In recognition of the state of flux within parts of the discipline we have not sought to provide only our view, or indeed the view of any author, as the fina word and, therefore, no article can be taken to represent the view of anyone other than the authors of the article at the time of writing. Views in some articles may contradict views in others; that is a reflectio of the state of the art and is common in science.

Although some articles in this work were created specificall with this book in mind, the vast majority of articles are from the *Wiley Encyclopedia of Forensic Science*.[1] The consequence of this is that there is inevitably some duplication of information. However, because we intend that each article can stand alone, we consider that such duplication, as exists, simply adds to the utility of the book.

Forensic science operates, by definition within a legal context. This creates several problems in creating a volume like this one. Different jurisdictions may have different legal requirements of the expert, and even the experts may have local practices that differ from other localities nationally or internationally. Even within the United States and United Kingdom, depending on the level of court, there are widely differing expectations and standards for the admissibility of scientifi evidence (e.g., Frye, Daubert, or none). We cannot expect to cover all of the variances and so the articles, other than where specificall addressing jurisdictional issues, should be taken as informing on the generality of practices.

The dichotomy between legal and scientifi standards is perhaps best illustrated in the NAS report of 2009;

> "The bottom line is simple: In a number of forensic science disciplines, forensic science professionals have yet to establish either the validity of their approach or the accuracy of their conclusions, and the courts have been utterly ineffective in addressing this problem. For a variety of reasons – including the rules governing the admissibility of forensic evidence, the applicable standards governing appellate review of trial court decisions, the limitations of the adversary process, and the common lack of scientifi expertise among judges and lawyers who must try to comprehend and evaluate forensic evidence – the legal system is ill-equipped to correct the problems of the forensic science community."

For those reasons, and others (e.g., availability of other evidence), we would caution (as have others) against using any court decision as validation or invalidation of any scientifi test. It is not unknown for different courts

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[1] www.wileyonlinelibrary.com/ref/efs

within the same jurisdiction to rule both ways on the same science; for example, the use of low template DNA in New York City.

Thus, this volume sets out to provide a comprehensive introduction to the scientific statistical, and legal issues within the context of forensic DNA profiling The rate of development of the field is so great that almost any publication will be out of date within a very short time. However, the information provided here will provide a solid foundation from which future developments can be understood and evaluated.

<div align="right">

Allan Jamieson
Scott Bader
July 2015

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Glossary

accreditation	recognition of procedural management at an institution
allele	one of alternative forms of a genetic marker, component/DNA type
amplificatio	increase in amount of sample DNA created by PCR process
amylase	enzyme of saliva, and to lesser extent some other body fluid
AP	Acid Phosphatase, detected by presumptive test for seminal fluid
base pair	building block unit of DNA
baseline	the experimental zero value on the x-axis of analytical results
bin	part of the epg showing known allelic sizes
body flui	usually refers to any biological material from which DNA can be obtained
buccal	derived from mouth cavity
cell	smallest living structure of biological organism
chromosome	structure containing DNA including many genes, inherited as a single unit from cell to cell and generation to generation
coancestry coefficien	a measure of the relatedness of two people
Daubert	legal standard for admissibility of expert evidence in some US states
degraded DNA	partially destroyed DNA, usually indicated by lower or absent amounts of longer DNA components
diploid	possessing two alleles at each locus
drop-in	appearance of DNA component in a profil due to background contamination
drop-out	disappearance of DNA component from a profil due to random sampling of low level quantity
electrophoresis	movement of chemical through a matrix under the force of electrical fiel

extraction	(in DNA casework) the removal of DNA from cells
Frye	legal standard for admissibility of expert evidence in some US states
genotype	genetic composition of an individual comprising both alleles at each/all loci
haploid	possessing only one allele at each locus
haplotype	genetic composition of an individual comprising one allele at each/all loci, linked together as a inherited group
hemizygous	only one allele component present at a locus
heterozygous	two alleles at one locus are different types
homozygous	two alleles at one locus are the same type
HWE	Hardy Weinberg Equilibrium, stable frequency of alleles
ISO17025	accreditation for the general requirements for the competence to carry out tests and/or calibrations, including sampling
ladder	(allelic) quality control sample containing alleles of known size and run separately to other samples
locus/loci (pl.)	specifi location/entity of DNA (marker or gene) on a chromosome, area of DNA tested in profil
low copy number (LCN)	very low amount (of DNA) in sample; specificall also the increased amplificatio cycle number used for PCR method
low template	very low amount (of DNA) in sample
micro	one millionth, 10^{-6}
milli	one thousandth, 10^{-3}
mitochondrion	intracellular structure containing mitochondrial DNA
mixture	more than one contributor (DNA profiling
multiplex	chemistry analysing many loci
mutation	alteration in genetic component
nano	one thousand millionth, 10^{-9}
nucleus	intracellular structure containing nuclear DNA (used in standard DNA profiling
odds	number of favourable outcomes/number of unfavourable outcomes

partial profil	one in which all of the components do not appear
Phadebas	presumptive test for saliva, detects amylase activity
phenotype	expressed/observed biological characteristic controlled by combination of alleles in genotype
pico	one million millionth, 10^{-12}
polygenic	controlled by several genes
polymerase	chemical that creates the amplificatio of DNA by PCR
polymorphic	many forms
population	in statistics, any set of items under study
presumptive	suggestive, not definit ve
primer	chemical that binds to specifi site (locus) of sample DNA to enable amplificatio in PCR
probability	number of favourable outcomes/number of possible unfavourable outcomes
pull-up	artifact seen in another part of DNA profil due to presence of a DNA component in one part of the profil
quantitation	measurement of the amount of a sample
rfu	relative fluorescenc unit, measurement of peak height in an electropherogram
saliva	body flui produced by salivary glands in mouth, containing salivary amylase
semen	body flui produced by male ejaculation, including seminal fluid and sperm cells
seminal flui	nutrient body flui secreted by prostate gland of males for transmission of sperm cells in ejaculate
sensitivity	(a) a measure of how small an amount of material a technique can detect (b) the effect on the signal or measurement of a change in an input ability to detect and measure a sample
specificit	ability to discriminate an individual component of a sample
sperm	male sexual cell present in semen, produced by testes, carrying haplotype of individual
stochastic	effect due to random variation caused by sampling of low level sample
stochastic threshold	approximate level at which random sampling effects can be expected

stutter   artifact seen in DNA profil as smaller peak adjacent to main peak of real DNA
                               component

validation   evidence of compliance/effica y for a process being fi for purpose, with
                               demonstration of capabilities and limits

x-axis   the horizontal axis of a graph

y-axis   the vertical axis of a graph

Abbreviations and Acronyms

A	adenine
AAFS	American Academy of Forensic Sciences
ABC	American Board of Criminalistics
ABI	Applied Biosystems
ACPO	Association of Chief Police Officers
ADO	allele dropout
AIMs	ancestry informative markers
AP	acid phosphatase
APA	American Psychological Association
ASCLD/LAB	American Society of Crime Laboratory Directors/Laboratory Accreditation Board
BKV	BK virus
bps	base pairs
C	cytosine
CCD	charged coupled device
CE	capillary electrophoresis
CF	cystic fibrosi
CODIS	Combined Offender DNA Index System
CPI	Combined Paternity Index
CPI	combined probability of inclusion
CZE	capillary zone electrophoresis
DAB	DNA Advisory Board
ds	double-stranded
DTT	dithiothreitol
EBV	Epstein–Barr virus
EDNAP	European DNA Profilin Group
emPCR	emulsion PCR
ENFSI	European Network of Forensic Science Institutes
EPG	electropherogram
ESS	European Standard Set
EVC	externally visible characteristics
FBI	Federal Bureau of Investigation
FSS	forensic science service
G	guanine
Hb	heterozygote balance ratio
HBV	hepatitis B virus
HHV-1	human herpes virus type 1
HIV-1	human immunodeficien y virus type 1
HLA	human leukocyte antigen
HPHR	heterozygous peak height ratio

HPLC	high-performance liquid chromatography
HPV	human papillomavirus
HV	hypervariable
HWE	Hardy Weinberg Equilibrium
IAI	International Association for Identificatio
IBD	identical-by-descent
IISNP	individual identificatio SNP
indel	insertion/deletion
ISFG	International Society for Forensic Genetics
ISO	International Standards Organization
JCV	polyomavirus JC
LCN	low copy number
LDO	locus dropout
LMD	laser microdissection
LoCIM	locus classificatio and inference of the major
LR	likelihood ratio
LT	low-template
LTDNA	low template deoxyribonucleic acid
MALDI/TOF	matrix-assisted laser desorption/ionization time-of-flight
MCMC	Monte Carlo Markov Chain
MDA	multiple displacement amplificatio
MGF	maternal grandfather
MGM	maternal grandmother
MHC	major histocompatibility complex
MLE	most likely estimate
MLP	multilocus probing
MP	match probability
mRNA	messenger RNA
mtDNA	mitochondrial deoxyribonucleic acid
MW	molecular weight
NAS	National Academy of Science (USA)
NCIDD	National Criminal identificatio DNA Database
NDIS	National DNA Index System
NDNAD	National DNA Database
NFI	Netherlands Forensic Institute
NGS	next-generation sequencing
NOAA	National Oceanic and Atmospheric Administration
NRC	National Research Council
nuDNA	nuclear deoxyribonucleic acid
OCME	Offic of the Chief Medical Examiner
PCR	polymerase chain reaction
PE	probability of exclusion
PGF	paternal grandfather
PGM	paternal grandmother
PHR	peak height ratio
PHT	peak-height threshold
PML	progressive multifocal leukoencephalopathy
PoD	probability of detection
POI	person of interest
PSA	prostate-specifi antigen

QA/QC	quality assurance and quality control
QAS	quality assurance standard
rCRS	revised Cambridge Reference Sequence
RFID	radio frequency identificatio
RFLP	restriction fragment length polymorphism
RFU	relative fluorescence unit
RHC	red hair color
RMNE	random man not excluded
RMP	random match probability
SBE	single-base extension
SDIS	State DNA Identificatio System
SDS	sodium dodecyl sulfate
SFGR	spotted fever group Rickettsia
SGM	second generation multiplex
SLP	single locus probes
SNP	single nucleotide polymorphism
SOP	standard operating protocol
SSM	slipped strand mispairing
STR	short tandem repeat
SWG	scientifi working group
SWGDAM	scientifi working group for DNA analysis methods
T	thymine
UV	ultraviolet
VNTR	variable number of tandem repeat
WGA	whole genome amplificatio
WTC	World Trade Center
YHRD	Y chromosome haplotype reference database

PART A
Background

Chapter 1
Introduction to Forensic Genetics

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The Ideal Forensic Material – Individualization

Forensic genetics has been touted as the gold standard of forensic analysis. This is because DNA fulfil many of the criteria that make the perfect forensic technology to establish a person's presence at a scene of crime.

Most forensic disciplines concerned with offences against the person, and some other crimes, try to establish a link between items found at the scene and items found on or associated with a suspect. In other words, to establish whether the recovered items could have originated from the same source. This process can be summarized as

1. Establishing a match
2. Calculating the significanc of the match

The perfect conclusion of this exercise is to unequivocally establish that the material from the crime scene could only have come from exactly the same source as that found on or associated with the suspect and no other source. The goal of most forensic matching is to reduce the potential population from which an item could have come, to one individual within the population. This extreme is the definitio of identification The process that we are more interested in, because of its more common application, is that of *individualization*. This is the process of individualization. Individualization is a population problem as it is necessary to be able to demonstrate how many people in a population may have the match characteristics discovered by the investigator. Therefore, modern scientifi individualization techniques recognize that most, if not

all, evidence is probabilistic, which is to say that we attempt to establish a *probability* or likelihood that two items had a common origin. The ideal forensic material must enable matching and probability calculations.

There are other qualities that a forensically useful material should have. *Ideally*, the material should be

1. Unique
2. Not change over time (i.e., during normal use)
3. Likely to be left at a scene in sufficien quantity to establish a match
4. Not change after being left at the scene and during subsequent examination

In this book, we shall see that DNA meets many, but not all, of these criteria and how the limitations are handled.

So what makes DNA a good material forensically?

DNA – The Molecule

DNA is sometimes called the *blueprint of life* and has characteristics that are appropriate to its role. Many, if not all, of these characteristics are important in Forensic Genetics, which is simply genetics in a legal context. These characteristics include its simplicity and yet complexity, both of which are incorporated within the polymeric chemical structure of the backbone molecule and the varied sequence of sidechain bases (the so-called letters of its information content), arranged in a double helix (*see DNA: An Overview*). The molecule is made from a relatively small number of building blocks yet contains a vast amount and range of information that can defin the nature of the biological cell, and ultimately the multicellular organism,

within which the DNA is located. The double helix structure is relatively stable in time yet is adaptable enough to "open up" to allow a living cell to use the contained information to go about its life functions (*transcription*) or to make copies of itself (*replication*). DNA is stable so as to enable transfer of the genetic information from generation to generation after replication (with cell division and mating where relevant), yet it can also change to varying extents. Some of the changes are important to only an individual organism and may be deleterious (e.g., mutation giving rise to a cancer), or are the basis for individual variation (e.g., mutation giving rise to a new variant, and the haploid segregation of chromosomes in gametes with the return of diploid pairing at fertilization to produce a new individual). Some changes affect a subpopulation (e.g., lineages) and even eventually an entire population (e.g., natural selection of mutations and new diploid combinations leading to evolutionary change).

The chapter on *DNA* describes some fundamental concepts about DNA and genetics. In summary, the genetic material of humans comprises about 3 billion nucleotides or building blocks, and is present in two copies per cell, so about 6 billion in total. This DNA is found within the nucleus of all cells other than red blood cells, in total it is called the *genome* and contains the genes that encode the proteins created by the cell to defin the cell's type and characteristics and ultimately the entire organism of the human individual. It also contains other DNA sequences that are regulatory (i.e., affect the temporal or quantitative expression of the genes), structural (i.e., affect intracellular packaging and stability of DNA), or are as yet of unknown function or may even be foreign to a normal human cell (e.g., a viral infection). All of these elements are contained within 23 separate lengths of DNA, the chromosomes.

The concept that DNA contains the information for biological life using a genetic code encoded within the sequence of bases along the double helix molecule means that if we as forensic scientists can "read" that code we can question and determine the source of a given sample of DNA. The general DNA structure and constituents are the same so that with the right analytical toolkits, we are able to answer that question. So, we could test not only whether the DNA is from a human, horse, cannabis plant, or soil microbe, but in theory identify the individual human. Scientists are able to take advantage of the "adaptable stability" of

DNA and mimic the process of replication so as to make multiple copies of a DNA sample, using the polymerase chain reaction (PCR, see method). The amplifie DNA is then processed and the data interpreted accordingly.

DNA in Populations

The first main concept to elaborate upon is that of Mendelian genetics (*see* Mendel mentioned in *DNA*). For a simple biological example, I will use the ABO blood group system. Here, there is a single gene involved that define a person's blood group. The gene controls the production of a chemical on the surface of blood cells. The gene exists within the human population in one of three forms or variants: *A*, *B*, and *O*, and when referring to the gene, it is written italicized. The existence of variable forms within the population is called a *polymorphism*, and these genetic variants are known scientificall as *alleles*. They control the production of a protein that exists, respectively, as either protein variant A, variant B, or is not produced (i.e., absent) and thus called O (for null).

In any individual, the genes that encode everything that eventually produces a human being are present in two copies (not including the X and Y chromosomes), one inherited from mother and one inherited from father. It is the combination of the two copies of all the genes that will determine the fina characteristics of the individual. So, while there might be just the one gene for the blood cell protein described above, there will be two copies of the gene in each person. All of the possible genetic combinations seen in different individuals are therefore *AA, BB, OO, AB, AO, BO*, and where the variants are the same, the person is called *homozygous*, where they are different, the person is called *heterozygous*. Going back to the description of the proteins that would be produced from the genetic variants, they are as follows in the table:

Gene variants	Protein variants	Blood group
AA	A only	A
BB	B only	B
OO	Nothing	O
AB	A and B	AB
AO	A only	A
BO	B only	B