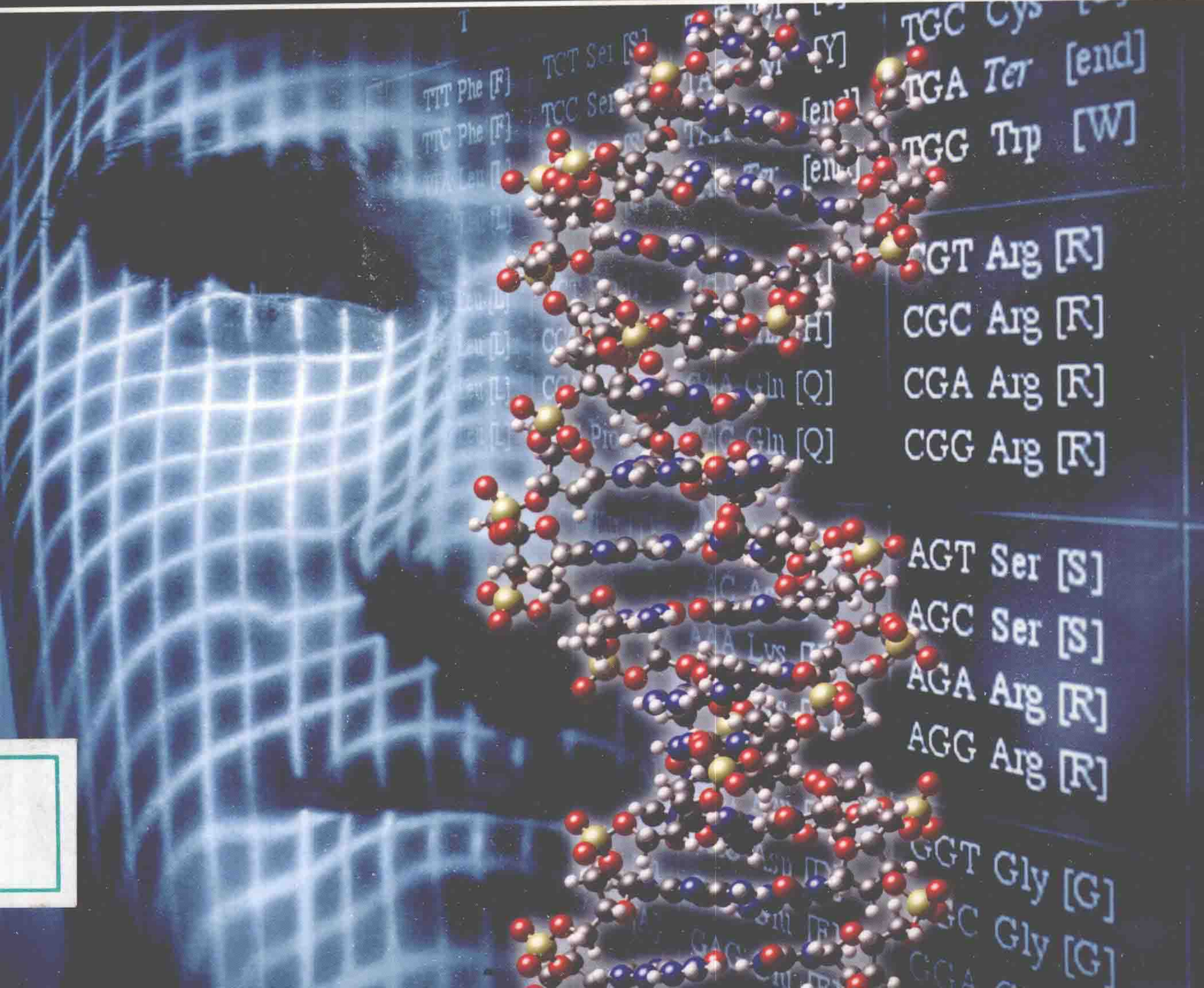
Calculations for Molecular Biology and Biotechnology

A Guide to Mathematics in the Laboratory

Frank H. Stephenson



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To my wife, Laurie, and our beautiful daughter, Myla.

Foreword

It was sometimes difficult for me to find a common ground with my high school chemistry teacher. We couldn't agree on what was appropriate attire or hair length for a sophomore. He had no respect for the notion that surfing is a viable career goal. He smoked way too much. But it was either in spite of him or because of him that I learned the mathematics involved in calculating the concentration of solutions, and I eventually agreed with him on the importance of numbers in the biological and chemical sciences. By the time I got out of that class, I was feeling as though I could have converted the speed of light into picomoles. As I undertook a career in molecular biology and teaching, it was what I learned in that class, more than in any other, that I have used on almost a daily basis.

Mathematics is a beautiful and elegant way of expressing order. I have heard it called a universal language. If true, then there are many dialects. There are any number of ways to approach a problem, no one of them necessarily more legitimate than another. I have always found interesting the passion and fervor people attach to their particular approach to mathematics. "Why do you do the problem **that** way?" I might be asked. "Clearly," my critic continues, "if you solve the problem **this** way, it's much quicker, more logical, and easier to follow. This is the only way that makes any sense." Well, maybe to them. Not everyone's brain works in the same way. In solving a problem in concentration, for example, it is probably amenable to solution by using a relationship of ratios, or $C_1V_1 = C_2V_2$, or the approach most often taken in this book. In actuality, they are all variations on a theme. Any one of them will get you the answer. Therein, I believe, lies the very beauty of mathematics.

It wasn't until this last year that I discovered the approach that I take to most of the problems encountered in the molecular biology laboratory has a name. It is called **dimensional analysis**. I always thought of it as "canceling terms." My brain is comfortable with this method. Many have tried to convert me to the use of the $C_1V_1 = C_2V_2$ approach, but all have failed. I have been chided and ridiculed by some for the manner in which I solve problems. I have been applauded by others. When I learned that the approach I take has the name **dimensional analysis**, I felt, in a way, like the person who visits the doctor with some inexplicable malady and who is reassured when the doctor attaches some Latin-sounding name to it. At least then, the individual knows that other people must also have the affliction, that it has been studied, and that there may even be a cure.

To present every possible way that each problem in this book could be solved would have made it too cumbersome. I make no apologies to those who might think that any one problem is better solved in another manner. To those of you who use this book as a companion in the laboratory, if you replace your values with the ones I have used in the example problems, you will do fine. You will have the numbers you need such that, for example, you will not be adding too little or too much salt that will send your cultured cells into osmotic shock or give you *Eco*RI star activity when digesting DNA.

My appreciation goes to my colleague Maria Abilock for bringing her critical eye to bear on this manuscript. She agreed to critique the draft in spite of the fact that she feels her way of solving problems is better than mine.

Frank H. Stephenson, Ph.D.

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Introduction

There are some 3,000,000,000 base pairs making up human genomic DNA within a haploid cell. If that DNA is isolated from such a cell, it will weigh approximately 0.0000000000035 grams. To amplify a specific segment of that purified DNA using the polymerase chain reaction (PCR), 0.00000000001 moles of each of two primers can be added to a reaction that can produce, following some 30 cycles of the PCR, over 1,000,000,000 copies of the target gene.

On a day-to-day basis, molecular biologists work with extremes of numbers far outside the experience of conventional life. To allow them to more easily cope with calculations involving extraordinary values, two shorthand methods have been adopted that bring both enormous and infinitesimal quantities back into the realm of manageability. These methods use scientific notation and metric prefixes. They require the use of exponents and an understanding of significant digits.

Significant Digits

Certain techniques in molecular biology, as in other disciplines of science, rely on types of instrumentation capable of providing precise measurements. An indication of the level of precision provided by any particular instrument is given by the number of digits expressed in its readout. The numerals of a measurement representing actual limits of precision are referred to as **significant digits**.

Although a zero can be as legitimate a value as the integers 1 through 9, significant digits are usually nonzero numerals. Without information on how a measurement was made or on the precision of the instrument used to make it, zeros to the left of the decimal point trailing one or more nonzero numerals are assumed not to be significant. For example, in stating that the human genome is 3,000,000,000 base pairs in length, the only significant digit in the number is the 3. The nine zeros are not significant. Likewise, zeros to the right of the decimal point preceding a set of nonzero numerals are assumed not to be significant. If we determine that the DNA within a sperm cell weighs 0.0000000000035 grams, only the 3 and the 5 are significant digits. The 11 zeros preceding these numerals are not significant.

Problem 1.1 How many significant digits are there in each of the following measurements?

a) 3,001,000,000 bp (base pairs)
b) 0.00304 grams
c) 0.000210 liters*
* Volume delivered with a calibrated micropipettor.

Solution 1.1

Given Number	Number of Significant Digits	The Significant Digits Are:
a) 3,001,000,000 bp	4	3001
b) 0.00304 grams	3	304
c) 0.000210 liters	3	210

Rounding Off Significant Digits in Calculations

When two or more measurements are used in a calculation, the result can only be as accurate as the least precise value. To accommodate this necessity, the number obtained as solution to a computation should be rounded off to reflect the weakest level of precision. The following guidelines will help determine the extent to which a numerical result should be rounded off.

Guidelines for Rounding Off Significant Digits

1. When adding or subtracting numbers, the result should be rounded off so that it has the same number of significant digits to the right of the decimal as that number used in the computation with the fewest significant digits to the right of the decimal.

2. When multiplying or dividing numbers, the result should be rounded off so that it contains only as many significant digits as that number in the calculation with the fewest significant digits.

Problem 1.2 Perform the following calculations, and express the answer using the guidelines for rounding off significant digits described in the preceding box.

a) 0.2884 g + 28.3 g
b) 3.4 cm × 8.115 cm
c) 1.2 L ÷ 0.155 L

Solution 1.2

a) 0.2884 g + 28.3 g = 28.5884 g

The sum is rounded off to show the same number of significant digits to the right of the decimal point as that number in the equation with the fewest significant digits to the right of the decimal point. (In this case, the value 28.3 has one significant digit to the right of the decimal point.)

28.5884 g is rounded off to 28.6 g.

b) 3.4 cm x 8.115 cm = 27.591 cm^2

The answer is rounded off to two significant digits since there are as few as two significant digits in one of the multiplied numbers (3.4 cm).

27.591 cm^2 is rounded off to 28 cm^2.

c) 1.2 L ÷ 0.155 L = 7.742 L

The quotient is rounded off to two significant digits since there are as few as two significant digits in one of the values (1.2 L) used in the equation.

7.742 L is rounded off to 7.7 L.

Exponents and Scientific Notation

An **exponent** is a number written above and to the right of (and smaller than) another number (called the **base**) to indicate the power to which the base is to be raised. Exponents of base 10 are used in scientific notation to express very large or vary small numbers in a shorthand form. For example, for the value 10^3, 10 is the base and 3 is the exponent. This means that 10 is multiplied by itself three times ($10^3 = 10 \times 10 \times 10 = 1000$). For numbers less than 1.0, a negative exponent is used to express values as a reciprocal of base 10. For example,

$$10^{-3} = \frac{1}{10^3} = \frac{1}{10 \times 10 \times 10} = \frac{1}{1000} = 0.001$$

Expressing Numbers in Scientific Notation

To express a number in scientific notation:

1. Move the decimal point to the right of the leftmost nonzero digit. Count the number of places the decimal has been moved from its original position.

2. Write the new number to include all numbers between the leftmost and rightmost significant (nonzero) figures. Drop all zeros lying outside these integers.

3. Place a multiplication sign and the number 10 to the right of the significant integers. Use an exponent to indicate the number of places the decimal point has been moved.
   a. For numbers greater than 10 (where the decimal was moved to the left), use a positive exponent.
   b. For numbers less than 1 (where the decimal was moved to the right), use a negative exponent.

Problem 1.3 Write the following numbers in scientific notation.

a) 3,001,000,000
b) 78
c) 60.23×10^{22}