RAPID ESTIMATION OF THEORETICAL COUNTER-CURRENT DISTRIBUTION VALUES

BY E. LEONG WAY AND BLAIR M. BENNETT

(From the Division of Pharmacology and Experimental Therapeutics and the College of Pharmacy, University of California, San Francisco, California, and the Department of Preventive Medicine and Public Health, School of Medicine, University of Washington, Seattle, Washington)

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The usefulness of the Craig counter-current distribution technique (1, 2) for studying the purity of compounds and the metabolic fate of therapeutic agents can be augmented by deriving the theoretical distribution values from the "Tables of the binomial probability distribution" (3). By use of such tables, which only recently have become generally available, laborious calculation of theoretical counter-current values can be reduced to a minimum. Thus, the plotting of theoretical distribution curves for any number of transfers in the manner described by Williamson and Craig (4) is greatly facilitated.

As proposed by Williamson and Craig (4), the fraction of a solute present in a given tube on completion of the fundamental procedure can be calculated by expanding the binomial

$$\left(\frac{1}{K+1} + \frac{K}{K+1}\right)^n$$

the individual terms of which may be denoted as

$$T_{n,r} = \frac{n!}{r!(n-r)!} \left(\frac{1}{K+1}\right)^r K^{n-r}$$

for $r = 0, 1, \ldots n$, where $T_{n,r}$ represents the fraction of the total material in the $r$th tube distributed through $n$ tubes, and $K$ is the distribution constant or partition ratio, expressed as the concentration of the solute in the upper phase over that of the lower phase. From one particular term, the successive terms may be determined by the relationships

$$T_r = \frac{n-r+1}{r} \cdot KT_{r-1}$$

or

$$T_r = \frac{r+1}{n-r} \cdot \frac{1}{K} \cdot T_{r+1}$$
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Obviously, the calculation of such terms for various values of $K$ is rather
laborious and becomes more involved with an increasing number of trans-
fers. Consequently, an approximate method of calculation is usually em-
ployed in such instances (3).

Lieberman (5), by use of a logarithmic expression for the recursion
formula (3), has reduced the computational labor to an appreciable extent.
By obtaining the logarithm of the initial term, $T_0$, the successive values of
log $T_r$ are then derived by simple addition. However, considerable com-
putation is still necessary and the method retains the disadvantage that
any initial error in computation will affect all subsequent calculations.
For example, in Lieberman's Table III for $K = 0.9$, the error made in
calculating the theoretical distribution for $r = 16$ persists through the
subsequent $r$ values calculated.

In contrast, by using the "Tables of the binomial probability distribu-
tion" (B. P. D. tables), once $n$ is specified, all the terms $T_{n,r}$ may be ob-
tained directly by reading columnwise across the table. Furthermore, in a
particular column for a specified $n$ and $r$, the corresponding terms for 50
derived values of $K$ are given, and, by a slight manipulation, an additional
50 values can be obtained. Since the values of the individual terms are
tabulated to seven decimal places, the accuracy is greater than that re-
quired experimentally.

In the B. P. D. tables are tabulated the $(n + 1)$ successive individual
terms of the binomial expansion

\[
\binom{n}{r} p^r q^{n-r}
\]

$r$ ranging from 0, 1, ... $n$ and $q = 1 - p$. This is simply another way of
expressing Equation 2 if, in particular, we set $p = K/(K + 1)$ and $q = 1/(K + 1)$.
It may be noted, of course, that the combinatorial factor $\binom{n}{r}$
is equal to $n!/(r!(n - r)!$. Thus we have for Equation 5

\[
\binom{n}{r} p^r q^{n-r} = \frac{n!}{r!(n-r)!} \left( \frac{K}{K+1} \right)^r \left( \frac{1}{K+1} \right)^{n-r} = \frac{n!}{r!(n-r)!} \left( \frac{1}{K+1} \right)^{K'} = T_{n,r}
\]

$T_{n,r}$ can be obtained, therefore, by direct reference to the B. P. D.
tables. It is only necessary then to adjust the values of $K$ to conform
with those of $p$ in the B. P. D. table. Thus, since $K = p/(1 - p) = (1 - q)/q$, when $p = 0.50 = q, K = 1.0$; likewise, when $p = 0.20, q = 0.80, K = 0.25$, etc. Since the range of $p$ and $q$ in the tables is from 0.01 to
0.50 at intervals of 0.01, it is possible to obtain 100 corresponding values
of $K$. These have been computed and the data are given in Table I.

If, for example, we wish to obtain the fraction for Tube 12 of twenty-
four transfers, for $K = 1$, this is equivalent to considering Equation 5,
evaluated for \( n = 24, r = 12, \) and \( p = 0.5 = q, \) or \( T_{24,12} = \binom{24}{12}(0.5)^{12} \times (0.5)^{12} = 0.1611802. \) Instead of direct calculation, the answer is obtained by merely referring to the B. P. D. tables for \( n = 24, r = 12, \) and \( p = 0.50. \)

In order to obtain the corresponding \( T_{n,r} \) for \( p \) greater than 0.50 (\( K > 1 \)),

**Table I**

*Calculated Values for \( K \)*

The values correspond to assigned values of probability, \( p, \) in "Tables of the binomial probability distribution." \( K = p/(1 - p) = (1 - q)/q. \)

<table>
<thead>
<tr>
<th>( p ) or ( q )</th>
<th>( K(&lt;1) )</th>
<th>( K(&gt;1) )</th>
<th>( p ) or ( q )</th>
<th>( K(&lt;1) )</th>
<th>( K(&gt;1) )</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.01</td>
<td>0.1010</td>
<td>99.000</td>
<td>0.26</td>
<td>0.3514</td>
<td>2.846</td>
</tr>
<tr>
<td>0.02</td>
<td>0.0204</td>
<td>49.000</td>
<td>0.27</td>
<td>0.3699</td>
<td>2.704</td>
</tr>
<tr>
<td>0.03</td>
<td>0.0309</td>
<td>32.333</td>
<td>0.29</td>
<td>0.3889</td>
<td>2.571</td>
</tr>
<tr>
<td>0.04</td>
<td>0.0417</td>
<td>24.000</td>
<td>0.30</td>
<td>0.4085</td>
<td>2.448</td>
</tr>
<tr>
<td>0.05</td>
<td>0.0526</td>
<td>19.000</td>
<td>0.31</td>
<td>0.4286</td>
<td>2.333</td>
</tr>
<tr>
<td>0.06</td>
<td>0.0638</td>
<td>15.667</td>
<td>0.32</td>
<td>0.4493</td>
<td>2.226</td>
</tr>
<tr>
<td>0.07</td>
<td>0.0753</td>
<td>13.286</td>
<td>0.33</td>
<td>0.4706</td>
<td>2.125</td>
</tr>
<tr>
<td>0.08</td>
<td>0.0870</td>
<td>11.500</td>
<td>0.34</td>
<td>0.4925</td>
<td>2.030</td>
</tr>
<tr>
<td>0.09</td>
<td>0.0989</td>
<td>10.111</td>
<td>0.35</td>
<td>0.5132</td>
<td>1.941</td>
</tr>
<tr>
<td>0.10</td>
<td>0.1111</td>
<td>9.000</td>
<td>0.36</td>
<td>0.5335</td>
<td>1.857</td>
</tr>
<tr>
<td>0.11</td>
<td>0.1236</td>
<td>8.091</td>
<td>0.37</td>
<td>0.5525</td>
<td>1.778</td>
</tr>
<tr>
<td>0.12</td>
<td>0.1364</td>
<td>7.333</td>
<td>0.38</td>
<td>0.5737</td>
<td>1.703</td>
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<tr>
<td>0.13</td>
<td>0.1494</td>
<td>6.692</td>
<td>0.39</td>
<td>0.6129</td>
<td>1.632</td>
</tr>
<tr>
<td>0.14</td>
<td>0.1628</td>
<td>6.143</td>
<td>0.40</td>
<td>0.6539</td>
<td>1.564</td>
</tr>
<tr>
<td>0.15</td>
<td>0.1765</td>
<td>5.667</td>
<td>0.41</td>
<td>0.6667</td>
<td>1.500</td>
</tr>
<tr>
<td>0.16</td>
<td>0.1905</td>
<td>5.250</td>
<td>0.42</td>
<td>0.6889</td>
<td>1.439</td>
</tr>
<tr>
<td>0.17</td>
<td>0.2048</td>
<td>4.882</td>
<td>0.43</td>
<td>0.7241</td>
<td>1.381</td>
</tr>
<tr>
<td>0.18</td>
<td>0.2195</td>
<td>4.556</td>
<td>0.44</td>
<td>0.7544</td>
<td>1.326</td>
</tr>
<tr>
<td>0.19</td>
<td>0.2346</td>
<td>4.263</td>
<td>0.45</td>
<td>0.7857</td>
<td>1.273</td>
</tr>
<tr>
<td>0.20</td>
<td>0.2500</td>
<td>4.000</td>
<td>0.46</td>
<td>0.8182</td>
<td>1.222</td>
</tr>
<tr>
<td>0.21</td>
<td>0.2658</td>
<td>3.762</td>
<td>0.47</td>
<td>0.8519</td>
<td>1.174</td>
</tr>
<tr>
<td>0.22</td>
<td>0.2821</td>
<td>3.545</td>
<td>0.48</td>
<td>0.8868</td>
<td>1.128</td>
</tr>
<tr>
<td>0.23</td>
<td>0.2987</td>
<td>3.348</td>
<td>0.49</td>
<td>0.9231</td>
<td>1.083</td>
</tr>
<tr>
<td>0.24</td>
<td>0.3158</td>
<td>3.167</td>
<td>0.50</td>
<td>0.9608</td>
<td>1.041</td>
</tr>
<tr>
<td>0.25</td>
<td>0.3333</td>
<td>3.000</td>
<td>0.51*</td>
<td>1.0000</td>
<td>1.000</td>
</tr>
</tbody>
</table>

* For \( p > 0.50 \) use \( q \) and the column \( K > 1 \).

since the expression \( \binom{r}{p}q^{n-r} \) is equal to \( \binom{n-r}{p}q^{n-r}p^r \), it is only necessary to interchange the values of \( p \) and \( q \) and those of \( r \) and \( (n - r) \) and then refer to the table with these revised values. Thus, if we require the term \( r = 16, n = 24, \) and \( K = 4 \) (\( p = 0.80 \)), it is easily seen that the B. P. D. table can be entered for the corresponding values \( r = 24 - 16 = 8, n = 24, \) and \( p = 1 - 0.80 = 0.20, \) and so the value for the term \( \binom{8}{4}(0.20)^8(0.80)^{16} \) is 0.0529963.
For any selected value of $K$ (or $p$) the successive fraction for any tube may be obtained by reading across columnwise for the respective $r$ values for a particular $n$. Furthermore, in any particular column, i.e. for a specified $n$ and $r$, we may also obtain all the $T_{n,r}$ values corresponding to various values of $K$ (or $p$). This gives a wide range of values for $K$ and allows for accurate plotting of theoretical distribution curves.

The range for $n$ in the B. P. D. tables is from 2 to 49. For counter-current distribution involving transfers in excess of forty-nine, as with the fifty-four plate machine, it is mentioned in the introduction to the tables that similar tables are available elsewhere for a range of $n$ from 1 to 150.

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SUMMARY

Theoretical counter-current distribution values were rapidly obtained from the "Tables of the binomial probability distribution" by merely adjusting partition ratios to conform with assigned values of the probability, $p$, in the tables. From these values a series of graphs can be plotted for any number of transfers in a counter-current distribution, thus obviating involved calculations in the fitting of any experimental curve.

BIBLIOGRAPHY

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E. Leong Way and Blair M. Bennett

J. Biol. Chem. 1951, 192:335-338.

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