

malleable, the most ductile and the most resistant to acid corrosion of all our metals. These properties could be put to work to-morrow. If so large a proportion of the world's gold supply finds its way into American vaults that its use as the basis of exchange between the nations is no longer practical and the European dictators make good their threat to force the world to abandon the gold standard permanently, there need be no fear of gold becoming a useless metal or of finding its only application in cheap jewelry. Chemical industry and our architects would be able to put the entire amount to immediate use and it is safe to predict that once the metal becomes available for commercial uses the demand for its unusual properties will prevent a collapse of the gold market.

Time does not permit consideration of the advances made in the last two decades in the chemistry of hydrogen, of oxygen, or sulfur, of phosphorus, of nitrogen, of chlorine, of bromine, of iodine, of fluorine, of silicon, of boron and of many other materials used by the inorganic chemist. The advances have been, in most cases, gradual and substantial rather than sudden and spectacular. But these changes have made material contributions to modern life. We live longer, we travel more rapidly, we move about more safely, we

are more secure, more comfortable, better fed and more effectively protected from contagion and more efficiently cured of disease because the research worker has been busily engaged in expanding the horizons of human knowledge.

Perhaps the most significant fact of all is the knowledge that each of these advances has opened out a new field which is ripe for the investigator. None of these developments must be regarded as complete, but as offering a new avenue for driving back the regions of superstition and ignorance. Inorganic chemistry, then, is not a worked-out field lacking worth-while problems for the research worker, but an area of ever widening interest, which is teeming with opportunity.

In closing may I call your attention to the fact that a survey of this type must either be incomplete or unbearably long. Perhaps it can be provocative without coming too close to either of these undesirable characteristics. If our minds have been stimulated and we are now willing to admit that inorganic chemistry has really made some worth-while advances within recent years and does actually contain some attractive problems which are still waiting solution, then perhaps we are ready to draw the conclusion that the golden age of research lies in the future and not in the past.

THE CONTROLLED EXPERIMENT AND THE FOUR-FOLD TABLE

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SUPPOSE that we are testing the potency of two viruses *A* and *B* by injecting dosages of each into six mice and find this result: Five of the mice receiving virus *A* die and one lives; one of the mice receiving virus *B* dies and five live. The question is regarding the statistical significance of the result judged by the usual criterion that $P = .05$ is the dividing line between significance and non-significance. Diagrammatically we may draw up the table

	died	lived	total
<i>A</i>	5	1	6
<i>B</i>	1	5	6
Total	6	6	12

As the numbers of mice in the *A* and in the *B* series are the same, as is often, if not usually, the case in such experiments, we may compare the numbers $n_A = 5$ and $n_B = 1$ which died by taking the difference $n_A - n_B = 4$. As the number which died in both series together is the same, namely 6, the assumption is made that the chance of death is $p = \frac{1}{2}$ and the chance of survival is $q = \frac{1}{2}$.

The question is asked: If $p = \frac{1}{2}$, is the chance for a difference $n_A - n_B$ so great as 4 (without regard to sign) less than .05? The usual method of answering this question is to find the standard deviation of $n_A - n_B$ as $\frac{1}{2} \sqrt{6+6} = \sqrt{3}$, and to consider that the difference is normally distributed with this standard deviation. Since the difference can take only integral values it is assumed¹ that the sum of the probabilities for $n_A - n_B$ as great as 4 is to be found from a table of the probability integral by considering the total area in the two tails beyond 3.5 (not beyond 4) when the standard deviation is $\sqrt{3}$. The ratio of 3.5 to $\sqrt{3}$ is 2.031 and the table gives $P = .0433$. The result is significant, though barely so.

A more careful calculation may be made by actually computing the probabilities for all the combinations of n_A and n_B which will make the difference numerically as great as 4. The chances for various values of n_A and n_B , when multiplied by $(1/2)^{12}$ are:

¹ See, P. R. Rider, "An Introduction to Modern Statistical Methods," pp. 71-72.

n_A	6	5	4	3	2	1	0
n_B	6	1	6	15	20	15	6
5	6	6	36	90	120	90	36
4	15	90	225	300	225	90	15
3	20	120	300	400	300	120	20
2	15	90	225	300	225	90	15
1	6	36	90	120	90	36	6
0	1	6	15	20	15	6	1

Along the main diagonal $n_A - n_B = 0$, along the diagonals next to the main diagonal it is ± 1 . The total chance for values as great numerically as 4 is found by adding up the northeast and southwest corners in each of which is

$$(15 + 36 + 15) + (6 + 6) + 1 = 79.$$

Then $2 \times 79 \div 2^{12} = .0386$. This is considerably less than the result obtained before, but is exact.

Sometimes one treats the data given by the experiment as a four-fold table and applies Chi-square. If we have a table

	died	lived	total
A	a	b	$a+b$
B	c	d	$c+d$
Total	$a+c$	$b+d$	N

Moreover in the four-fold table the number of degrees of freedom is 1 and χ is distributed in a normal curve with unit standard deviation so that it is merely necessary to find χ and use a probability integral table.² In the particular case under consideration $\chi^2 = 5 \frac{1}{3}$, $\chi = 2.309$, and $P = .0208$. This is very much less than the true value .0386. As a matter of fact it is known that if σ be the standard deviation of $n_A - n_B$, we have identically

$$\chi^2 = \left(\frac{n_A - n_B}{\sigma} \right)^2$$

and that the value for P obtained from χ^2 is precisely that which would be obtained from the ratio of $n_A - n_B$ to σ under the assumption that we used the actual value 4, instead of the value 3.5 as above, in forming the ratio; indeed $4/\sqrt{3} = 2.309$.

When the numbers of the four-fold table are small, we are advised to apply χ^2 with the Yates correction, viz.,

$$\chi_y^2 = \frac{N \left(|ad - bc| - \frac{1}{2}N \right)^2}{(a+b)(a+c)(c+d)(b+d)}.$$

In our case this gives $\chi_y^2 = 3$, $\chi_y = 1.732$, and $P = .0832$. This value is very much larger than the others and would, in fact, lead to the conclusion that the results of the experiment were not significant. We may, however, remember that when the numbers in a four-fold table are small, even the Yates correction may fail to give the correct probabilities and we must have recourse to R. A. Fisher's "Exact Method."³ If this be applied to the present table we have

² See Rider, *op. cit.*, p. 112.

³ See Rider, *op. cit.*, pp. 113-114, or R. A. Fisher, "Sta-

$$P = 2 \frac{6!6!6!6!}{12!} \left(\frac{1}{6!6!0!0!} + \frac{1}{5!5!1!1!} \right) = 37/462 = .0801$$

Thus the value of P obtained by the exact method of treating the four-fold table, though very near to the value indicated by χ^2_y with the Yates correction, is very far indeed from the values of the probability $P = .0386$ for a difference $n_A - n_B$ as large numerically as 4.

To pass from this illustration to a more general case, if the numbers in the experiment and its control are equal and of value n , and if $p = \frac{1}{2}$, the distribution of $n_A - n_B$ is strictly upon a point-binomial with $\sigma = \frac{1}{2}\sqrt{2n}$ and a range of $2n$, because the sums in the $2n+1$ diagonals of the $n \times n$ square made up of the elements

$$\frac{n!}{k!(n-k)!} \cdot \frac{n!}{l!(n-l)!}, \quad k+l=0,1,\dots,2n,$$

(as in the case above for $n=6$) are precisely the $2n+1$ binomial coefficients in the expansion of $(x+y)^{2n}$, as may be seen by multiplying $(x+y)^n(x+y)^n$ and collecting the term $x^{k+1}y^{2n-k-1}$. Thus the exact value of the probability for any run like

	died	lived	total
A	a	b	n
B	b	a	n
Total	n	n	$2n$

may be obtained by summing the first $2b+1$ terms of the point-binomial expansion of $(\frac{1}{2} + \frac{1}{2})^{2n}$ and doubling the result, it being assumed that $b < a$. An approximate result may be obtained by forming the ratio

$$(a-b-\frac{1}{2}) : \frac{1}{2}\sqrt{2n},$$

provided $b < a$, and looking up the corresponding probability in a probability-integral table.

On the other hand, the exact value of the probability if the table is treated as a four-fold table may be obtained from the series

$$\frac{n!n!}{2n!} \left\{ 1^2, n^2, \left[\frac{n(n-1)}{2} \right]^2, \dots, \left[\frac{n(n-1)}{2} \right]^2, n^2, 1^2 \right\}$$
 of the squares of the coefficients of the binomial expansion of the n th power, by summing the first $b+1$ terms and doubling the result for such is indeed the value of

$$P = 2 \frac{n!n!n!n!}{(2n)!} \left[\frac{1}{n!n!0!0!} + \frac{1}{(n-1)!(n-1)!1!1!} + \dots + \frac{1}{a!a!b!b!} \right].$$

This value of P will be very close to the value determined by figuring Chi-square with the Yates correction, but will be considerably larger than the value of the probability computed for the difference $a-b$ or less.

In the following table are given for a variety of four-fold tables the values of the probability for (1) the difference $a-b$ or greater, (2) the same as estimated from $(a-b-\frac{1}{2}) : \frac{1}{2}\sqrt{2n}$, (3) the given four-fold table or worse by R. A. Fisher's exact method, (4) the estimate by χ^2 , (5) the estimate by χ^2_y .

	point-binomial		four-fold table		
	(1) exact	(2) $\frac{(a-b-\frac{1}{2})}{\sigma}$	(3) exact	(4) χ^2	(5) χ^2_y
3, 0 0, 3	.031	.041	.100	.014	.103
5, 1 1, 5	.0386	.0433	.0801	.0208	.0832
9, 3 3, 9	.0226	.0246	.0392	.0141	.0413
18, 10 10, 18	.0440	.0450	.0604	.0326	.0613
19, 11 11, 19	.0519	.0529	.0698	.0388	.0706

From this table it appears that the value of the probability for a difference as great as $a-b$ may be obtained with a fair degree of approximation from the probability-integral as in column (2); but that the value obtained from χ^2 is far too low and the value obtained from χ^2_y is far too high, as is also that obtained from the four-fold table by the exact method, —even when the numbers in the table are fairly large. Indeed it may be inferred that until the numbers have become so large that the values of P computed from χ^2 and χ^2_y are satisfactorily near together, neither of these values are satisfactory. Even for a table with $a=110$, $b=90$ we have $P=.0456$ from χ^2 and $P=.0574$ from χ^2_y , the former about 11 per cent. below and the latter about 11 per cent. above the true value of P . As an experiment and control are usually run on fairly small numbers it is clear that the data may not be treated by the methods applicable to the four-fold table.

Only the simplest case has been discussed, the one where the numbers (of mice) in the two runs are equal and where the data make $p=\frac{1}{2}$ for experiment and control together. If we have a table such as

	died	lived	total
A	6	2	8
B	1	5	6
Total	7	7	14

for which the numbers are different, but the value of p remains $\frac{1}{2}$, we are already in difficulties. We may not compare the numbers that died but have to compare the proportions $6/8=.75$ and $1/6=.167$. The value of χ^2 leads to $P=.0308$ whereas that of χ^2_y leads to $P=.1052$. If we compute the chance of an equally bad four-fold table by the exact method we have $P=.1026$ which is close to the value given by χ^2_y . If we obtain

$p_A-p_B=7/12$ and its standard deviation $\sigma=\sqrt{42}/24$ and their ratio $\sqrt{42}/3=2.160$ we come back, as we must, upon the value $P=.0308$ given by χ^2 .

To find the actual distribution of p_A-p_B it is necessary to form the products

$$\frac{1}{2^6} \frac{6!}{k!(6-k)!} \cdot \frac{1}{2^8} \frac{8!}{l!(8-l)!}$$

for all values of k from 6 to 0 and of l from 8 to 0 and to collect the results according to p_A-p_B , of which the values advance by $1/24=.04167$. The distribution is, of course, symmetric; it turns out to be as follows for positive values of p_A-p_B :

24(p_A-p_B)	0	1	2	3	4	5	6	7
2 ¹⁴ chance	1402	888	588	1128	1056	456	588	840
24(p_A-p_B)	8	9	10	11	12	13	14	15
2 ¹⁴ chance	435	216	420	336	90	120	168	56
24(p_A-p_B)	16	17	18	19	20	21	22	23
2 ¹⁴ chance	15	48	28	0	6	8	0	1

It will be observed that the distribution is not unimodal but very irregular. The particular value of p_A-p_B given in the table is $14/24$. Summing the actual chances we have 330 for positive values as great as $14/24$ and the same for negative values, so that the true value of P for so large a difference in the proportion of deaths in experiment and control is $P=660/2^{14}$, which is .0403, and the difference is significant. As the distribution is centered at the multiples of $1/24$, it would seem as though we should use instead of $14/24$ for p_A-p_B the value $14/24-\frac{1}{2}/24=27/48$ relative to $\sigma=\sqrt{42}/24$ when consulting a table of the probability-integral. The resulting value of P is .0373, which is not far from the value obtained by summation.

We must not, however, expect that any simple modi-

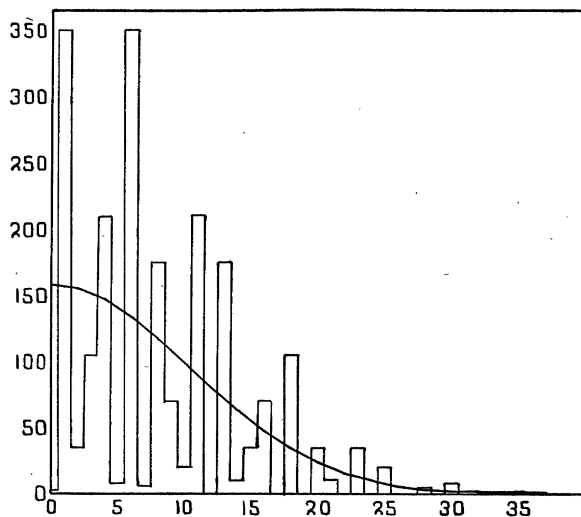


FIG. 1. Histogram of the chance ($\times 2^{12}$) for different values of p_A-p_B ($\times 35$) when there are 7 animals in one series and 5 in the other, with $p=q=\frac{1}{2}$, and normal curve of the same standard deviation.

fication of $p_A - p_B$ will afford, relative to σ , a value as a normal deviate which will give a good value for P , because the great irregularity in the distribution of $p_A - p_B$ makes it impossible to fit any normal curve at all closely to the values of the chances for different values of $p_A - p_B$. Fig. 1 shows the distribution when we have 7 in one series and 5 in the other, where the differences advance by $1/35$, and also the normal curve which "fits" in the sense that its standard deviation is that of $p_A - p_B$. With the great oscillations on the two sides of the curve, it must be clear that the summation of the chances to a given abscissa can not be expected to be closely equal to the area under the curve.

It may be remarked that for the experiment with its control we do not logically have a four-fold table to be

treated as that table usually is treated. What we have is two independent point-binomials. Moreover, what a χ^2 -table gives us is the chance for an observed table as bad as we have, *i.e.*, for one of equal or less probability (apart from fluctuations due to small numbers). But the probabilities of the different tables are not in the same serial order as the differences $p_A - p_B$ in the different tables. Hence there is neither logical nor arithmetic likelihood that the use of χ^2 should solve well our problem of determining whether the effects of treatment in experiment and control are statistically significant. It is still true, of course, that if numbers are sufficiently large, χ^2 will give the correct probabilities, but they have to be larger than is customary in such experiments.

SCIENTIFIC EVENTS

THE SCIENTIFIC EXHIBITION AT DALLAS

THE American Association for the Advancement of Science, under the presidency of Dr. Irving Langmuir, associate director of research of the General Electric Company, will meet at Dallas, Texas, from December 29, 1941, to January 3, 1942, inclusive.

Fourteen sections of the Association and twenty-nine of its associated and affiliated groups will actively participate in the meeting. Among these groups will be the American Society of Zoologists, the Botanical Society of America, the American Society of Naturalists, the American Phytopathological Society, the Genetics Society of America, the American Meteorological Society and the American Society of Parasitologists.

The Adolphus and Baker Hotels, located diagonally across the street from each other, will serve as joint headquarters. The association registration and the annual exhibition will be on the mezzanine floor of the Baker Hotel. Most of the sessions will be held in the downtown section of Dallas, many being scheduled for the headquarters hotels.

The Texas Academy of Science and the Southwestern Division of the association, active in preparations for the meeting, are anticipating a large attendance from southwestern United States. The vast resources of this area, including cheap natural gas, and its easy accessibility to all parts of the United States have attracted large industries, and defense operations have stimulated many older industries, including the smelting of tin and zinc, the mining of mercury, extraction of magnesium and bromine from sea water; production of toluol, manufacture of paper, of airplanes and the building of ships. Scientists in these and other industries will contribute to the program of the meeting, and it is expected that many of the industries will be represented at the exhibition.

Announcements and diagrams of the exhibition hall

will be mailed to prospective exhibitors at the end of June. For information regarding exhibits, write to the undersigned, 3941 Grand Central Terminal, New York, N. Y.

DORIS LEISEN,
Director of Exhibits

THE PEARL DIVERS GROUP IN THE AMERICAN MUSEUM OF NATURAL HISTORY

THE new Pearl Divers Group in the Hall of Ocean Life at the American Museum of Natural History was opened on June 10. It was constructed under the direction of Dr. Roy Waldo Miner, curator of the Department of Living Invertebrates. It represents an underseas scene in the enclosed pearl lagoon of the coral atoll of Tongareva—a small ring-shaped island in the South Seas about 2,000 miles due south of Honolulu.

Through the large central opening of the group, which measures 35 feet across the front, 12 feet in depth and 14 feet in height, two Tongarevan pearl divers are depicted plunging down into a coral gorge beneath the water's surface.

One of the central features of the group is a cluster of pearl oysters adhering to the coral of the sea bottom. One of the native divers is gathering oysters to bring them to the surface, while the other is swimming down to reach the oyster bed. These are the large pearl oysters, with shells six to eight inches in diameter, that the world uses for knife handles, buttons, inlays and other decorations.

A bed of *Tridacna* clams (known as "man-trap" clams) is half buried in the rocky slope which rises to the cliff-like coral wall at the left, their sinuous openings gaily festooned with brightly colored mantle edges. This species of *Tridacna* is smaller than the