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Discovery and Re-Discovery of Antibiotics : A Further Study.

A Neelameghan, I K Ravichandra Rao, and **B S S Gupta*** *Documentation Research and Training Centre, Indian Statistical Institute, Bangalore* 3.

[The linear relation between the number of discoveries and the number of re-discoveries in the field of antibiotics conforms to the Square-Cube Law as applied to growing organisms. The Square-Cube Law relation gives a more precise prediction of the number of re-discoveries of antibiotics given the number of reports of discoveries of antibiotics, than with the least square technique, reported earlier. There is isometry between the relative rate of growth of the cumulative total number of discoveries and the cumulative total of the number of re-discoveries.]

1 Scope of the Paper

This paper reports further work in the series on patterns in discovery and rediscovery (7, 8, 9). In a case study in the field of antibiotics, it was shown that there is a linear relation between the number of discoveries and the number of re-discoveries. In the present paper we report that

1 The above-mentioned relationship between discovery and re-discovery conforms to the Square-Cube Law as applied to growing organisms;

2 The Square-Cube Law relation gives a more precise prediction of the number of reports of re-discovery of antibiotics, given the number of reports of discovery of antibiotics;

3 There is isometry between the relative rate of growth of the cumulative total number of discoveries and the cumulative total number of re-discoveries.

2 Square-Cube Law

The Square-Cube Law of growing organisms states that a linear correlation exists between the cube-root of the mass of an organism and the square-root of its surface area. This law

* Present address: Computer Centre, MI & AS Division, Air India, Santa Cruz East, Bombay 29.

has been shown to be applicable to the pattern of growth of industrial organisation (1, 2, 4–6). For example, defining the mass as the number of personnel having contacts within the organisation ("internal" employees) and the surface area as the number of personnel whose job call for contact with persons external to the organisation ("external" employees), a linear relationship was found to exist between the cube-root of the number of "internal" employees and the square root of the number of "external" employees. Refinements in the application of the law to industrial organisations have also been suggested.

3 Application to Discovery of Antibiotics

31 Notation

The following notation has been used:

X_t = Number of reported discoveries of antibiotics in year t

Z_t = Number of re-discoveries in year t

x_t = Square-root of X_t

z_t = Cube-root of Z_t

It will be noted that x_t and z_t are taken as the independent variable and dependent variable respectively. In this paper, as has been done earlier, the discovery of an antibiotic is considered a duplication if it is identified with another antibiotic and so reported in published documents, irrespective of whether the compounds were produced by one and the same or different species of micro-organisms.

32 Data

Table 1 in Sec 321 presents year-wise data on reports of discovery and of re-discovery of antibiotics.

321 *Table* 1. *Year-wise data on reports of discovery and duplication*

SN	Year	X_t	Z_t	x_t	z_t	z_t
1	1937	2	1	1·41	1·00	0·59
	1938	3	1	1·73	1·00	0·68
3	1939	8	0	2·83		1·00
4	1940	5	3	2·24	1·44	0·83
5	1941	3	0	1·73	0	0·68

SN	Year	X_t	Z_t	x_t	z_t	z_t
6	1942	15	8	3·87	2·00	1·30
7	1943	10	4	3·16	1·59	1·10
8	1944	20	7	4·47	1·91	1·48
9	1945	25	8	5·00	2·00	1·63
10	1946	27	2	5·2	1·26	1·69
11	1947	54	19	7·35	2·67	2·32
12	1948	44	8	6·63	2·00	2·11
13	1949	51	16	7·14	2·52	2·25
14	1950	42	12	6·48	2·29	2·06
15	1951	53	16	7·28	2·52	2·29
16	1952	58	12	7·62	2·29	2·39
17	1953	68	14	8·25	2·41	2·58
18	1954	84	22	9·16	2·80	2·84
19	1955	82	22	9·06	2·80	2·81
20	1956	72	24	8·49	2·88	2·65
21	1957	119	28	10·91	3·04	3·35
22	1958	79	22	8·89	2·80	2·76
23	1959	95	25	9·75	2·92	3·01
24	1960	89	20	9·43	2·71	2·92
25	1961	62	17	7·87	2·57	2·47
26	1962	93	26	9·64	2·96	2·80
27	1963	107	30	10·34	3·11	3·18
28	1964	100	20	10·00	2·71	3·08
29	1965	83	23	9·11	2·84	2·83
30	1966	77	17	8·83	2·57	2·75
$n = 30$		1630	427			

33 CORRELATION

The correlation coefficient (r) determined for each of the pairs of variables (X_t, Z_t) and (x_t, z_t) is 0·8404 and 0·9843 respectively. ($1 - r^2$) estimates the amount of variance of Z_t that is not associated with the linear regression on X_t. Therefore, r^2 is the amount of variance of Z_t due its regression on X_t. For the pairs of variables (X_t, Z_t) and (x_t, z_t) the value of r^2 is 0·6978 and 0·9678 respectively. Thus, about 70 per cent of the variance of Z_t is due to its linear regression on X_t; and about 97 per cent of the variance of z_t is due to its linear regression on x_t.

$b = \Sigma xy/\Sigma x^2$ where

x and y are the deviations from the mean. Thus,

$$b = 0 \cdot 2909$$

$$\hat{z}_t = \bar{z}_t + b\,(x_t - \bar{x}_t)$$

$$\hat{z}_t = 0 \cdot 2909\, x_t + 0 \cdot 1769.$$

4 Testing of Hypothesis

The Null Hypothesis $H_0: \beta_0 = 0$, that there is no linear relationship between x and y was tested against the Null Hypothesis $H_1: \beta_1 \neq 0$, that there is linear relationship between x and y. The calculated value of $t = 11 \cdot 91$. At 1 per cent level the table value of df of t with $n - 2 = 28$ is $2 \cdot 763$ (10). Thus, the Null Hypothesis $H_0: \beta_0 = 0$ was rejected indicating a linear relationship between x_t and z_t.

5 More Precise Predictability

In Sec 33 it has been mentioned that the correlation coefficient for (X_t, Z_t) is $0 \cdot 8404$ and that for (x_t, z_t) is $0 \cdot 9843$. Thus, the use of the Square-Cube law with x_t and z_t gives a more precise prediction of the duplication of discoveries for a particular year than the use of the relationship between X_t and Z_t for the purpose (8).

6 Isometry

Studies on the attributes of growth — such as, growth-in-time, relative growth, and isometry — are helpful in predicting the trend of growth of a system and its components.

61 HUXLEY'S METHOD

Huxley's method (3) to study the relative growth of a whole organism with respect to its organ or that between two organs of the same organism, by plotting the logarithm of the measurement of an attribute of the respective variables, can be generalised. Thus, if Y is the measurement of the attribute of a component and X that of the whole or of another component of the same system, then $d \log Y / d \log X = k$, the allometric coefficient, representing the ratio of the relative growth of the pairs of entities is said to be isometric. The isometry is in the positive or negative direction according as $k > 1$ or $k < 1$. Huxley's method was used for studying the relative rate of growth of pairs of variables among the following three variables: Cumulative total number of discoveries (X); (2) Cumulative total number of new discoveries (Y), and (3) Cumulative total number of re-discoveries in the field of antibiotics for the 30-year period 1937–66.

62 DATA

Year-wise data on the number of discoveries (X_t) and of re-discoveries (Z_t) are given in Table 1 in Sec 321. The number of new discoveries in a year (Y_t) is given by $Y_t = X_t - Z_t$.

63 ALLOMETRIC COEFFICIENT

The data were grouped into periods of 3, 5 and 6 years for determining the allometric coefficient (k) between the pairs (X,Y) (X,Z), and (Y,X). The respective values of k is given in the following table.

Pair of variables	Allometric coefficient k for		
	3-year	5-year	6-year
X,Y	0·0997	0·9945	1·0375
X,Z	1·0304	1·0172	0·9104
Y,Z	1·0220	1·0219	0·8828

7 Observation

The value of k is very nearly equal to 1 in each of the cases indicating an isometric relationship between the respective pairs of variables considered. It is further noted that the value of k for the 3-year and 5-year periods is closer to 1 than that for the 6-year period.

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