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KINETICS OF URINARY EXCRETION RATE FROM THE VIEWPOINT OF THE ALMOST-ONE PARAMETER HYPOTHESIS

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The almost-one parameter hypothesis is shown diagrammatically on the next page.

Since the last example in this diagram has not been reported thus far, we give here two examples.

We denote the natural logarithm of the excretion rate by X.

I. *500mg* Aspirin aluminum sugar coated tablet with(A) and without(B) antacid.

Table 1. $1.0 \le T_{max} \le 5.0$ *(hrs)*. Salicylates are measured.

The first fundamental relation (I) is tested as the regression equation of $X_i(t)$ on $X.(t)$ for the range $6.0 \le t \le 19.5$ *(hrs)*. Fig. A.1 through B.6. Black spots in these figures are points for the range $0.25 \le t \le 5$ *(hrs)*.

	A.1	A.2	A.3	A.4
b_i	0.916 ± 0.039	0.822 ± 0.037	0.690 ± 0.040	1.547 ± 0.051
a_i	0.272 ± 0.118	0.790 ± 0.110	1.109 ± 0.119	-2.042 ± 0.153
	A.5	A.6	B.1	B.2
b_i	1.224 ± 0.102	1.167 ± 0.043	1.011 ± 0.063	0.888 ± 0.039
a_i	-0.594 ± 0.304	-0.446 ± 0.128	0.101 ± 0.189	0.443 ± 0.118
	B.3	B.4	B.5	B.6
b_i	0.479 ± 0.081	1.152 ± 0.017	0.991 ± 0.106	1.132 ± 0.081
a_i	1.775 ± 0.243	-0.447 ± 0.050	0.059 ± 0.319	-0.951 ± 0.243

Table 2

The estimate of $\rho(a_i, b_i) = -0.984$.

The second fundamental relation (II) holds also well, i.e.

$$s_x(t) = 0.915 - 0.202X.(t)$$
$$\pm 0.103 \pm 0.034$$

The correlation coefficient P between $X.(t)$ and $s_x(t)$ is equal to (-0.947), which is satisfactory.

THE ALMOST-ONE PARAMETER HYPOTHESIS

THE BIOLOGICAL PROCESS $X(t)$ IS PRIMITIVE, OR FUNDAMENTAL FOR THE LIFE.

THE INDIVIDUAL VARIABILITY OF $X_i(t)$ FOR $i = 1, 2, \ldots, N$ IS SUFFICIENTLY SMALL, WHERE THE VARIABILITY IS REPRESENTED BY A DIMENSIONLESS MEASURE. N NEED NOT BE SUFFICIENTLY LARGE.

THE i-TH INDIVIDUAL PROCESS IS A LINEAR FUNCTION OF THE REFERENCE PROCESS, I.E.

$$X_i(t) = a_i + b_i X.(t) \quad \ldots (I)$$

WITH NATURAL CONDITIONS

$a. = 0$, AND $b. = 1$,

THE DOT DENOTES THE MEAN WITH RESPECT TO i.

THE STANDARD DEVIATION OF $X_i(t)$ WITH RESPECT TO i, SAY $s_x(t)$, IS A LINEAR FUNCTION OF THE MEAN $X.(t)$, NAMELY

$$s_x(t) = \pm\ [s_a - s_b X.(t)] \quad \ldots (II),$$

WHERE s_a AND s_b DENOTE THE STANDARD DEVIATIONS OF a_i AND b_i RESPECTIVELY.

IN REALITY, TWO FUNDAMENTAL RELATIONS (I) AND (II) HOLD ONLY APPROXIMATELY, SO THAT WE SAY 'ALMOST-ONE PARAMETER' INSTEAD OF 'ONE PARAMETER'.

(IF NECESSARY, $X(t)$ IS TRANSFORMED IN ADVANCE INTO A NEW VARIATE, WHICH IS DENOTED AGAIN BY $X(t)$.)

ONE (GENETIC) FACTOR IS PREDOMINENT IN THE PROCESS.

PARAMETERS CONTAINED IN THE EXPLICIT FORM OF $X_i(t)$ ARE MUTUALLY DEPENDENT.

THE CORRELATION COEFFICIENT ρ BETWEEN a_i AND b_i IS EQUAL TO -1.

THERE EXISTS A CONSTANT C SUCH THAT

$a_i = C(1 - b_i)$.

THE PATH OF $X_i(t)$ PASSES A FIXED POINT (C, C) ON THE $X.$-X_i PLANE, WHEN t IS A CONTINUOUS PARAMETER.

EXAMPLES:

- STATURE, BUT NOT CHEST GIRTH, NOR WEIGHT.
- TIBIAL HEIGHT, FOOT LENGTH (WITH FOOT-BINDING EFFECT).
- LENGTH OF LONG BONE, SUCH AS FEMUR, TIBIA ETC.
- AGE AT ERUPTION OF TOOTH.
- METABOLIC PROCESS OF DRUG IN BLOOD.
- URINARY EXCRETION RATE OF DRUG.

ln(Salicylates excretion rate)

	Subj.	0.25 hrs	1.0	2.0	3.0	4.0	5.0	6.0	7.25	9.0	11.0	13.5	19.5	*r*
A		2.599	3.771	3.910	3.937	3.725	3.656	3.661	3.736	3.315	2.851	2.460	1.253	0.996
	2	2.527	3.321	3.408	3.813	3.752	3.741	3.738	3.786	3.576	3.288	2.805	1.587	0.996
	3	2.981	3.559	3.806	3.685	3.484	3.724	3.638	3.600	3.384	3.196	2.875	1.753	0.993
	4	3.216	4.181	4.068	4.094	3.537	4.097	3.851	3.489	3.036	2.594	1.647	-0.446	0.998
	5	2.377	3.877	3.956	4.027	3.725	3.852	3.894	3.609	3.871	3.027	2.299	0.637	0.986
	6	3.229	4.161	4.227	3.515	4.159	3.998	4.008	3.709	3.473	3.044	2.205	0.815	0.997
B	1	2.375	3.810	3.963	3.921	3.784	3.771	3.950	3.676	3.347	2.798	2.460	1.099	0.992
	2	3.085	3.927	3.727	4.158	4.037	3.798	3.775	3.656	3.529	3.002	2.431	1.430	0.996
	3	2.790	3.947	3.806	3.736	3.658	3.541	3.740	3.634	3.264	3.053	2.712	2.427	0.947
	4	2.373	3.676	3.663	4.077	3.597	4.154	3.846	3.759	3.374	3.017	2.244	0.761	1.000
	5	2.433	3.941	3.907	3.942	4.010	4.194	3.403	3.733	3.520	3.280	2.316	1.033	0.978
	6	3.103	4.183	4.340	3.807	4.179	4.283	3.113	3.483	2.713	2.313	1.778	0.239	0.990

($\rho = -0.984$)

Table 1

ln(Furosemide excretion rate)

		0.25 hrs	0.75	1.5	2.5	3.5	4.5	5.5	7	9	11	13	19	*r*
Subj.	1	4.595	9.020	8.738	8.536	7.421	6.644	6.136	5.313	4.564	3.738	3.135	0.956	0.994
	2	5.846	7.914	8.613	7.943	7.182	6.730	6.096	5.886	5.050	4.466	4.078	2.398	
	3	5.572	7.432	7.396	8.549	8.366	7.903	6.592	5.537	4.762	3.689	2.639	2.197	
A	4	5.938	7.610	7.636	7.434	8.526	7.917	7.057	6.438	5.642	4.970	4.533	4.644	
	5	5.846	7.426	7.474	8.104	8.347	7.607	6.908	6.654	5.730	5.011	4.595	3.367	
	6	5.649	8.338	7.611	7.408	6.778	6.319	6.073	5.403	4.868	4.431	4.489	3.807	0.968
	7	4.682	6.382	7.176	7.748	8.714	7.191	7.521	7.343	6.443	6.091	5.328	3.989	
	8	8.308	8.678	8.264	7.816	6.774	6.500	6.524	6.190	5.371	5.198	4.007	1.946	0.966
	1	7.497	8.891	8.412	7.497	7.323	6.951	6.987	6.555	5.919	5.037	4.317	2.833	0.990
	2	5.663	8.938	8.723	7.563	6.744	6.515	6.315	5.226	4.605	4.159	3.526	2.565	0.993
	3	4.060	6.375	7.209	7.360	8.712	8.021	7.098	6.314	5.384	4.533	4.159	2.565	
C	4	6.706	8.785	7.954	7.353	6.946	6.652	6.246	5.517	4.605	4.205	3.951	2.890	0.983
	5	4.234	5.897	8.487	7.867	7.247	6.757	6.229	5.883	5.513	4.754	4.394	3.689	
	6	2.079	8.827	8.696	7.625	7.088	6.609	6.685	6.258	5.656	4.905	3.871	3.332	0.988
	7	3.178	6.654	7.997	8.409	7.854	7.376	6.650	6.170	5.553	4.868	4.407	2.485	
	8	5.875	8.907	8.635	7.544	6.671	6.535	6.192	5.545	4.394	3.871	2.565	2.197	0.987

($\rho = -0.971$)

Table 3

II. *40mg* Furosemide tablet. Table 3. A & C stand for two brand names.

Subjects for the following analysis are so selected that $T_{max} = 0.75$ *(hrs)* and individual series of data, which is clearly bimodal, or contains zero, is excluded.

The regression equation of $X_i(t)$ on $X.(t)$ is applied to the range $3.5 \leq t \leq 19$ *(hrs)*. Fig. FA.1 through FC.8. Black spots in these figures are points for the range $0.25 \leq t \leq 2.5$ *(hrs)*.

	FA.1	FA.6	FA.8	FC.1
b_i	1.363 ± 0.060	0.659 ± 0.070	1.032 ± 0.113	1.010 ± 0.060
a_i	-2.325 ± 0.324	1.855 ± 0.376	0.034 ± 0.608	0.506 ± 0.324
	FC.2	**FC.4**	**FC.6**	**FC.8**
b_i	0.981 ± 0.046	0.954 ± 0.073	0.892 ± 0.057	1.134 ± 0.075
a_i	-0.123 ± 0.247	0.222 ± 0.395	0.930 ± 0.306	-1.130 ± 0.405

Table 4

The estimate of $\rho(a_i, b_i) = -0.971$.

The second fundamental relation (II) is given by

$$s_x(t) = \underset{\pm 0.098}{1.212} - \underset{\pm 0.018}{0.140} X.(t)$$

The correlation coefficient P between $X.(t)$ and $s_x(t)$ is equal to (-0.952).

The excretion rate of a drug, or its metabolites, depends not only its concentration in blood, but also on the pH of urine and others, so that regression equations are not necessarily equal for the identical subject, namely FA.8 & FC.1, or FA.1 & FC.2.

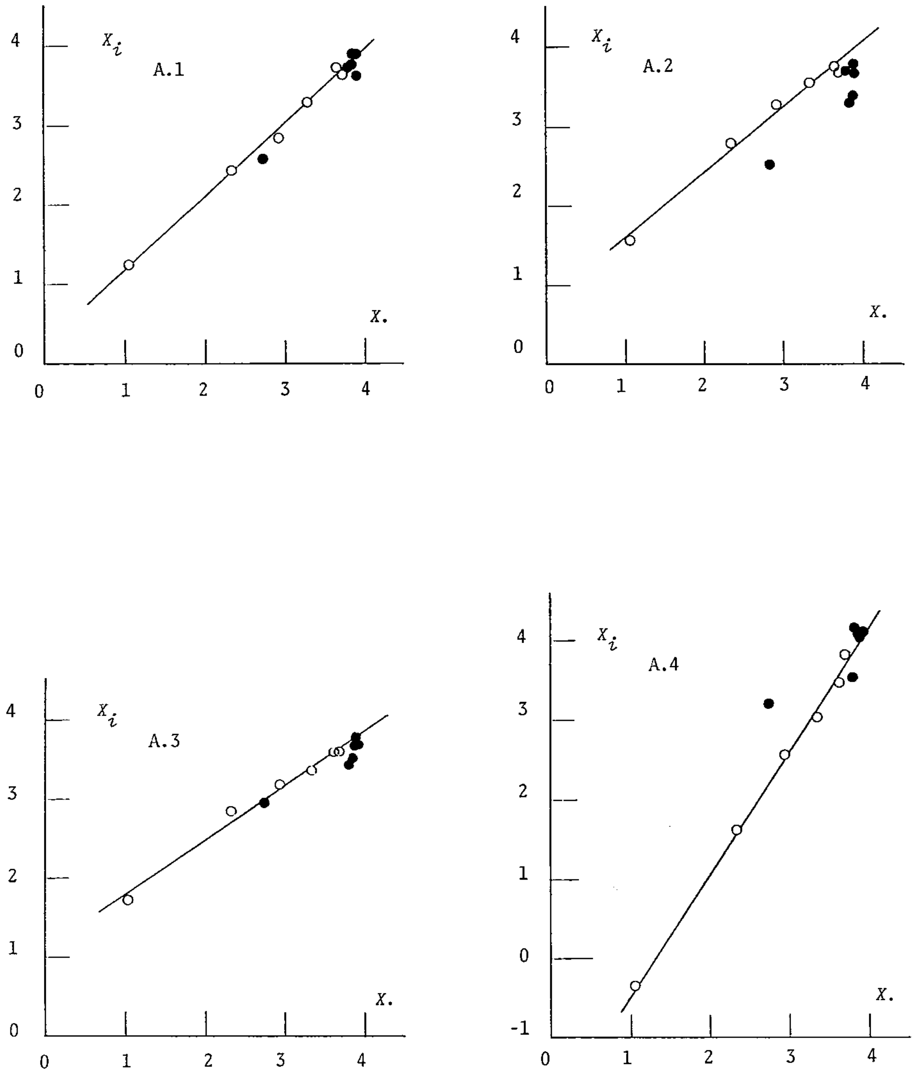

Fig. 1a

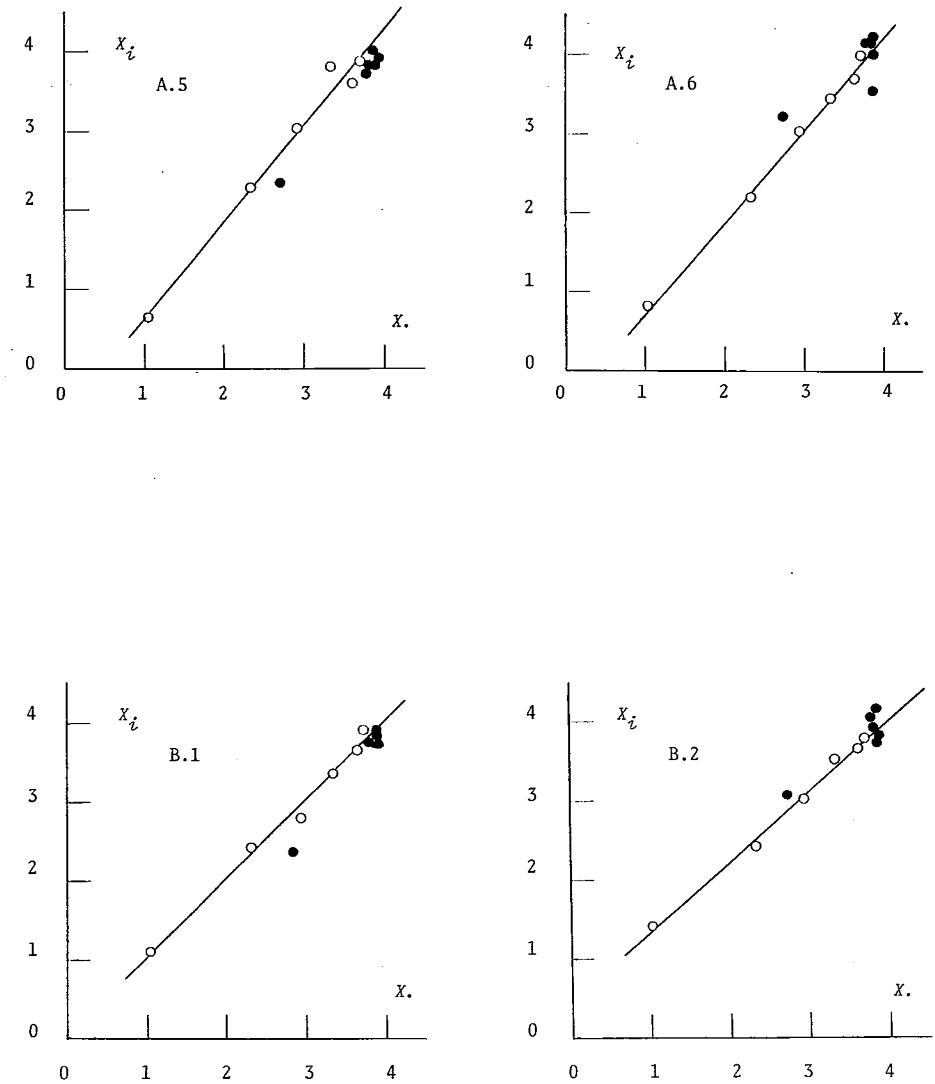

Fig. 1b

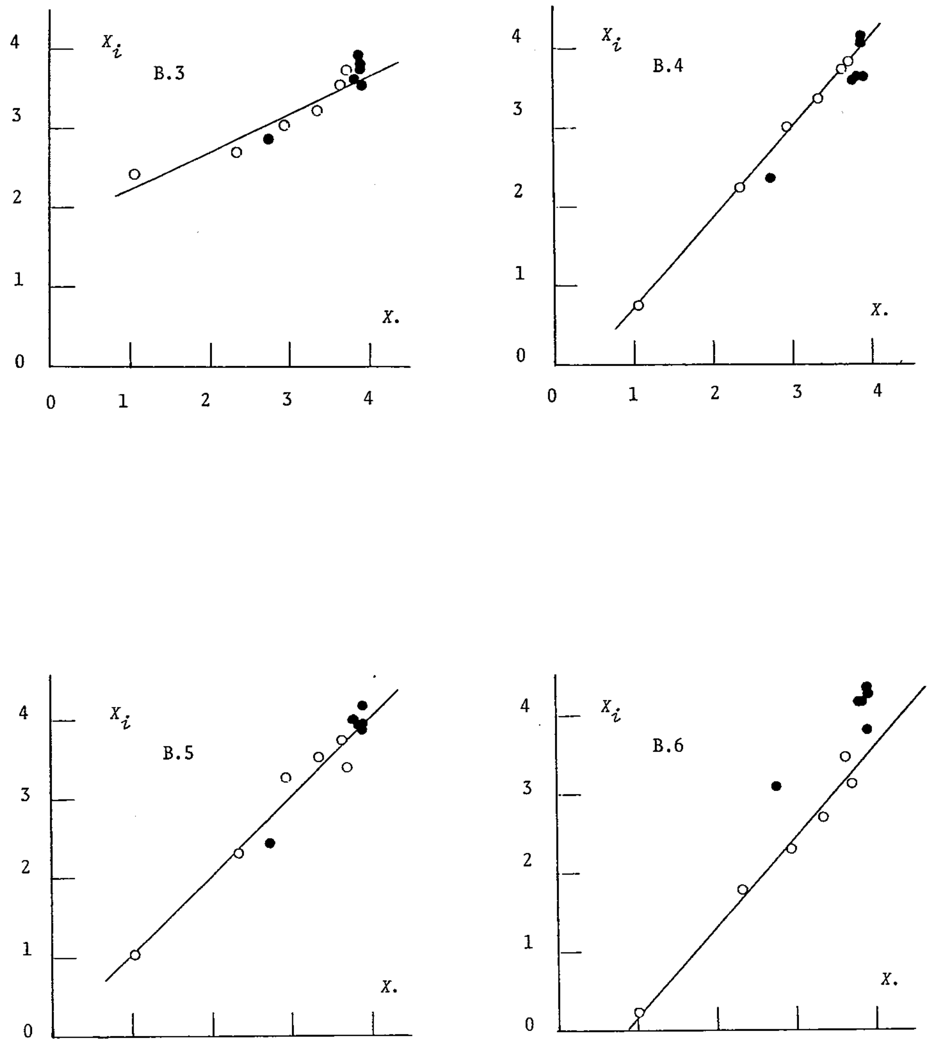

Fig. 1c

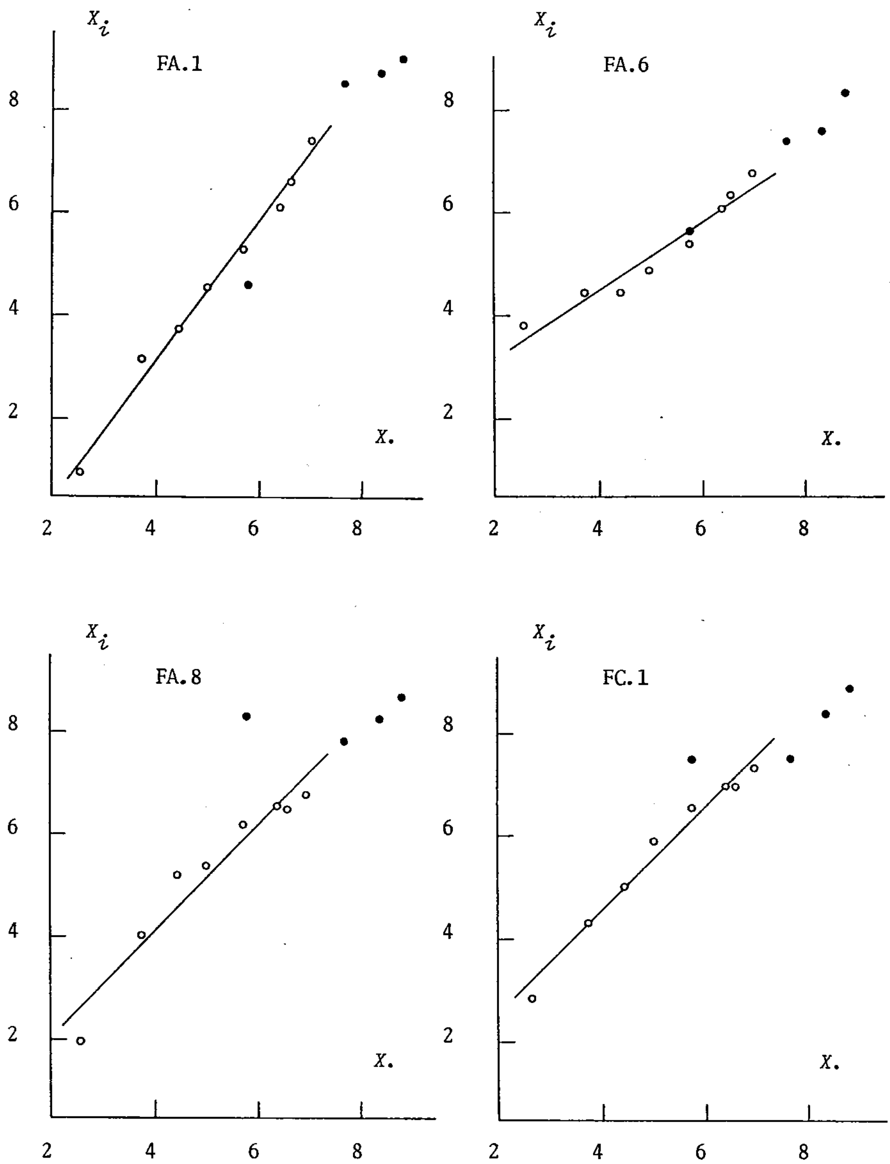

Fig. 2a

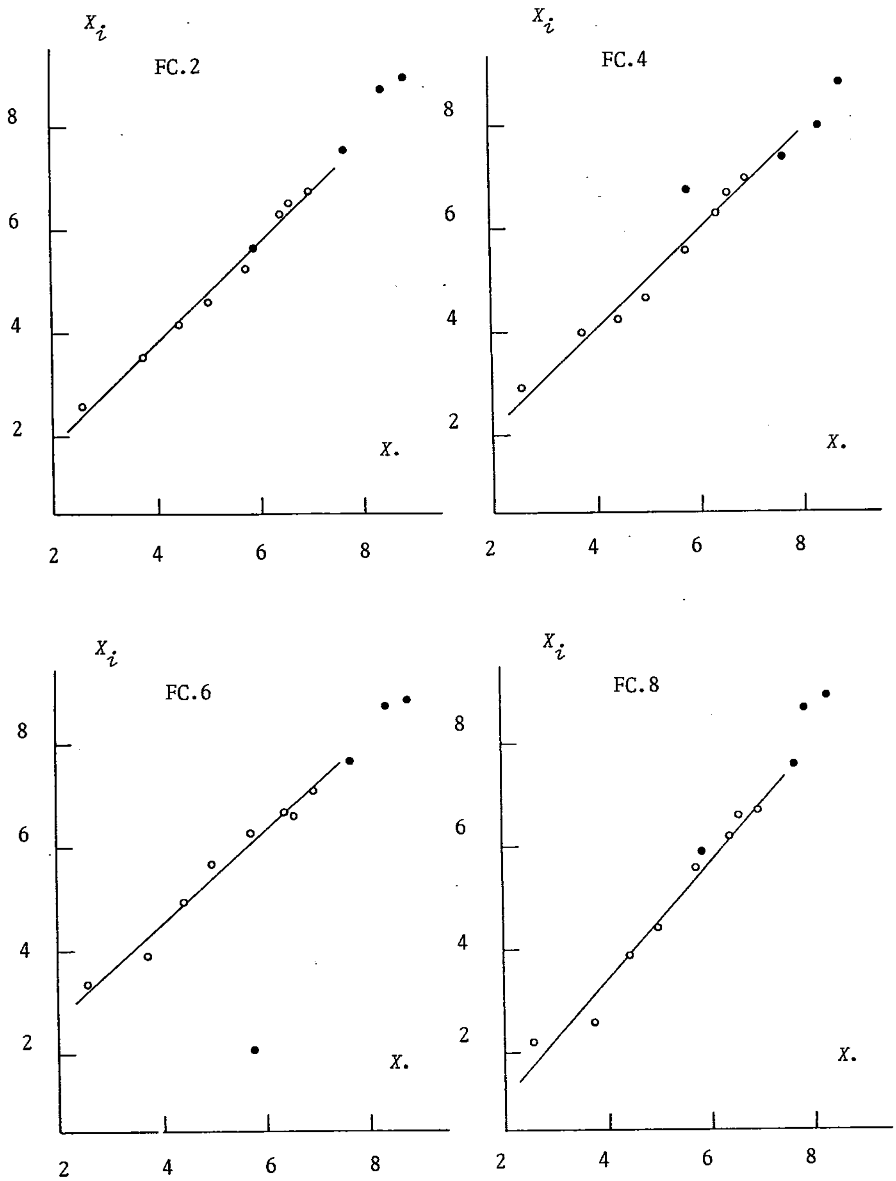

Fig. 2b

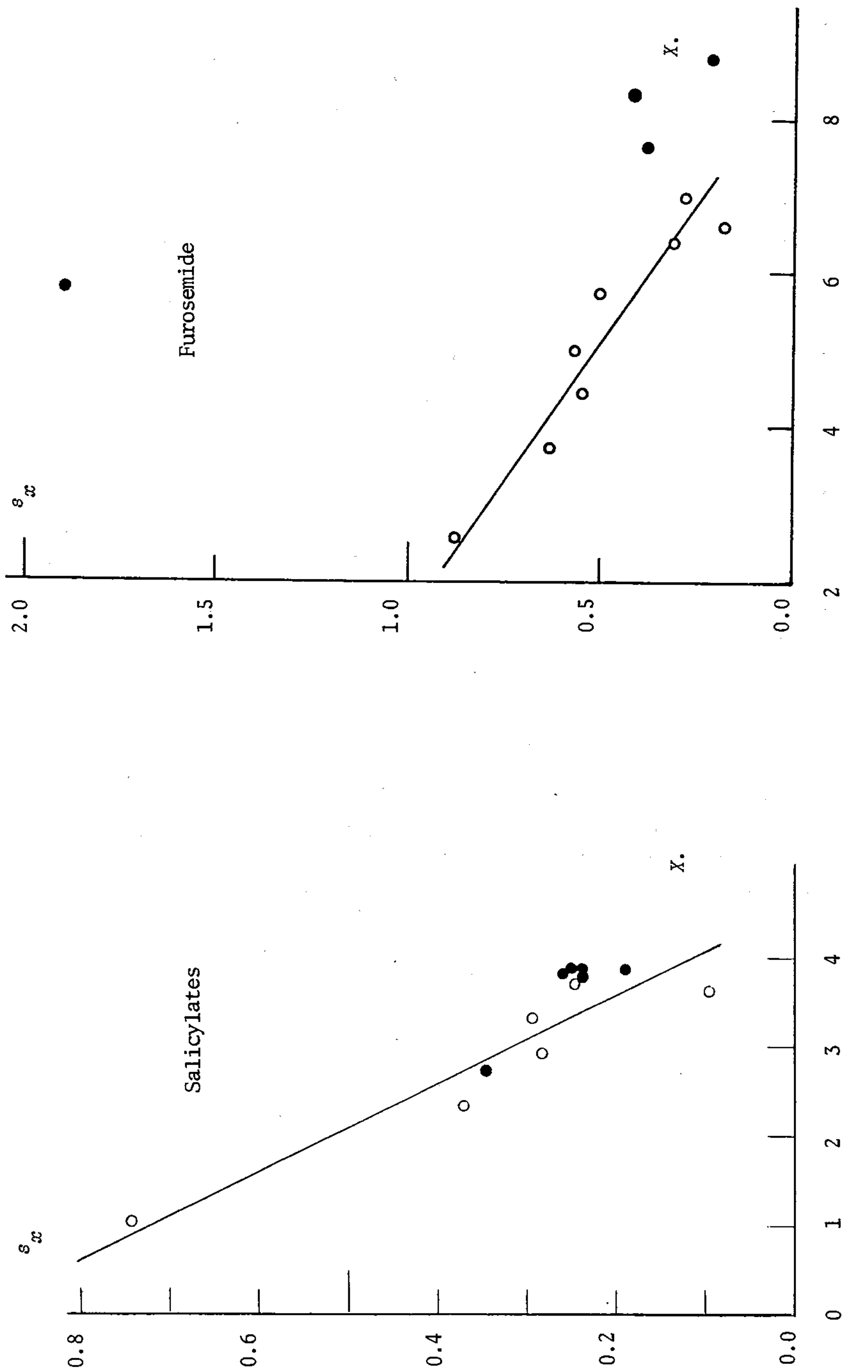
Furosemide
s_x
X.
2.0
1.5
1.0
0.5
0.0
2
4
6
8
Salicylates
s_x
X.
0.8
0.6
0.4
0.2
0.0
0
1
2
3
4

Fig. 3

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