GENETIC STRUCTURE OF HUMAN POPULATIONS

III. DIFFERENTIATION OF ABO BLOOD GROUP GENE FREQUENCIES IN SMALL AREAS OF JAPAN*

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1. INTRODUCTION

In a previous paper (Nei and Imaizumi, 1966a) it was shown that the local differentiation of *ABO* and *MN* blood group gene frequencies in Japan has occurred largely by genetic random drift. In that investigation the population of Japan was divided into 45 different sub-populations or *Prefectures* (administrative units of Japan) the sizes of which were mostly one to two millions. However, the size of mating groups of neighbourhoods in Wright's (1946) sense appears to be much smaller than the sub-populations employed in the paper. It is, therefore, expected that the gene frequencies are locally differentiated even within these sub-populations. We thus examined the degree of differentiation of *ABO* blood group gene frequencies in several small areas of Japan.

2. DIFFERENTIATION WITHIN PREFECTURES

There are two *Prefectures*, in which the local variation of *ABO* blood group gene frequencies can be analysed. One is Kagoshima Prefecture in Kyushu Island and the other Tokushima Prefecture in Shikoku Island (cf. fig. 1 in Nei and Imaizumi, 1966a). The data on the former were collected by Ono and Takagi (1942) and Makisumi (1958), and those on the latter by Katayama (1935) and Minamibuchi (1939). The areas of Kagoshima and Tokushima Prefectures are 9,104 km² and 4,143 km² respectively, both including several neighbouring small islands. The population sizes of these two Prefectures at the time of 1960 census are 1,962,998 and 847,279 respectively. Blood group typing was made on 6,926 individuals at 16 different locations in Kagoshima Prefecture and on 3,467 individuals at 14 different locations in Tokushima Prefecture. The locations at which blood group typing was made are given in figs. 1 and 2. These locations represent *mura*, *machi*, or *city*, administrative units smaller than Prefecture in Japan.

The frequencies of the gene I^A , I^B , and I^O controlling the *ABO* blood groups were estimated by Berenstein's method (cf. Nei and Imaizumi, 1966a). The results obtained are given in table 1, in which

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the frequencies of I^A , I^B , and I^O are denoted by p , q , and r respectively. In Kagoshima Prefecture, the χ^2 -value for the departure from the Hardy-Weinberg equilibrium is significant at the 5 per cent. level in one of the 16 sub-populations, whereas, in Tokushima Prefecture, it is significant at the same level in one of the 14 sub-populations. Thus, the

FIG. 1.—Geographical distribution of the locations for blood group typing in Kagoshima Prefecture.

observed phenotype frequencies agree fairly well with the theoretical expectations. The χ^2 for the heterogeneity of gene frequencies among the sub-populations is 79.2 with 30 degrees of freedom in Kagoshima Prefecture and 88.0 with 26 degrees of freedom, both of which are significant at the 0.1 per cent. level.

The degree of differentiation of gene frequencies may be measured by the inbreeding coefficient of sub-populations relative to the total

population. This inbreeding coefficient can be estimated from the means and genetic variances and covariances, as described by Nei and Imaizumi (1966*a*). The estimates of the inbreeding coefficient thus obtained are set out in table 2. The inbreeding coefficients averaged over all alleles and allele combinations for Kagoshima and Tokushima are both larger than the value previously obtained for the whole of Japan, *i.e.* 0.0007 (*cf.* Nei and Imaizumi, 1966*a*). This may be due

FIG. 2.—Geographical distribution of the locations for blood group typing in Tokushima Prefecture.

to the fact that the sizes of sub-populations employed for the whole of Japan were much larger than those for the present investigation, as will be discussed later. Table 2 also indicates that the inbreeding coefficient or f_{ST} is more variable in Tokushima than in Kagoshima according to the allele or allele combination concerned. This suggests that the differentiation of gene frequencies has not occurred at random, but the possibility of sampling accident cannot also be ruled out. To test the significance of individual values of f_{ST} from 0, an approximate χ^2 was computed by the following formula

$$\chi^2 = SS/\sigma_{\delta p}^2$$

where SS stands for the weighted sum of squares of the gene frequency concerned and $\sigma_{\hat{p}}^2$ for the mean sampling variance of gene frequency estimate (*cf.* Nei and Imaizumi, 1966a). The number of degrees of freedom of this χ^2 is equal to the number of sub-populations minus one. Note that the χ^2 is based on the assumption of independent distribution

TABLE 1

ABO blood group frequencies and estimates of gene frequencies in sub-populations of Kagoshima and Tokushima Prefectures

(i) Kagoshima Prefecture

Sub-population	N_s	Blood group frequency				Gene frequency			
		<i>O</i>	<i>A</i>	<i>B</i>	<i>AB</i>	<i>p</i>	<i>q</i>	<i>r</i>	χ^2
Kaseda	452	32.1	41.4	19.4	7.1	0.283	0.144	0.573	1.0
Ata	500	36.0	40.6	18.4	5.0	0.264	0.126	0.610	3.2
Kasasa	377	39.5	37.9	18.3	4.3	0.241	0.121	0.638	2.4
Boodomari	505	32.7	46.7	14.3	6.3	0.316	0.109	0.575	0.4
Chiran	517	30.0	40.4	22.6	7.0	0.277	0.162	0.561	4.0
Izaku	316	26.9	44.0	19.6	9.5	0.319	0.158	0.523	0.2
Beppu	327	32.4	45.0	15.6	7.0	0.307	0.121	0.572	0.1
Kawanabe	304	30.9	49.7	13.5	5.9	0.335	0.103	0.562	0.7
Ibusuki	318	25.2	50.9	15.7	8.2	0.363	0.128	0.509	0.8
Aira	379	29.0	40.4	20.8	9.8	0.294	0.167	0.539	0.0
Mizobe	565	29.7	43.6	17.7	9.0	0.311	0.144	0.545	0.0
Makizono	721	27.7	46.5	16.5	9.3	0.335	0.138	0.527	0.0
Kirishima	789	29.7	42.6	18.6	9.1	0.305	0.150	0.545	0.0
Takasu	312	31.1	39.8	20.8	8.3	0.280	0.159	0.561	0.2
Shibushi	297	30.3	40.4	18.9	10.4	0.298	0.158	0.544	0.5
Sueyoshi	247	27.1	44.1	20.7	8.1	0.311	0.157	0.532	1.2
Total*	6,926	30.7	43.3	18.2	7.8	0.302	0.141	0.557	5.5

(ii) Tokushima Prefecture

Sub-population	N_s	<i>O</i>	<i>A</i>	<i>B</i>	<i>AB</i>	<i>p</i>	<i>q</i>	<i>r</i>	χ^2
Tokushima	467	22.3	45.0	22.0	10.7	0.337	0.181	0.482	1.6
Kamajima	242	30.2	38.8	20.3	10.7	0.289	0.168	0.543	0.4
Kawata	137	24.1	39.4	21.9	14.6	0.319	0.202	0.479	0.6
Miyama	77	29.9	40.2	18.2	11.7	0.305	0.161	0.534	0.5
Shishikui	132	22.0	42.4	22.0	13.6	0.337	0.197	0.466	0.0
Orono	333	24.3	42.4	22.2	11.1	0.319	0.184	0.497	0.2
Aioi	221	32.6	41.6	19.0	6.8	0.283	0.139	0.578	0.5
Fukuhara	411	31.6	49.6	12.7	6.1	0.335	0.099	0.566	0.3
Sakashukito	196	30.6	48.0	15.8	5.6	0.321	0.114	0.565	3.1
Nakakito	89	32.6	48.3	11.2	7.9	0.336	0.100	0.564	0.3
Kamikito	87	29.9	49.4	12.6	8.1	0.347	0.109	0.544	0.0
Ichiu	181	28.2	50.3	13.8	7.7	0.353	0.114	0.533	0.0
Furumiya	158	17.7	39.3	34.8	8.2	0.283	0.253	0.464	8.1
Matsushima	736	31.5	39.0	20.3	9.2	0.280	0.160	0.560	0.1
Total*	3,467	28.0	43.3	19.5	9.2	0.312	0.157	0.531	1.4

* Gene frequencies in the row of "Total" refer to the weighted means.
 N_s = sample size.

of different gene frequencies, which is true only for a large number of multiple alleles. At any rate, the χ^2 thus obtained indicates that, in Tokushima, one of the three estimates of f_{ST} , *i.e.* that obtained from the frequency of I^A , is not statistically significant, whereas, in Kagoshima, all of the three estimates are significant (table 3).

TABLE 2

Means, genetic variances, and degrees of differentiation of gene frequencies in Kagoshima and Tokushima Prefectures

Alleles concerned	Kagoshima			Tokushima		
	Mean frequency	σ_{ij}	f_{ST}	Mean frequency	σ_{ij}	f_{ST}
I^A	0.3023	0.000474	0.00225	0.3124	0.000128	0.00060
I^B	0.1404	0.000187	0.00155	0.1567	0.001186	0.00897
I^O	0.5573	0.000605	0.00245	0.5309	0.000836	0.00336
I^A, I^B		-0.000025	0.00060		-0.000239	0.00488
I^A, I^O		-0.000443	0.00263		0.000111	-0.00067
I^B, I^O		-0.000158	0.00202		-0.000947	0.01138
Mean			0.00192			0.00475

σ_{ij} = genetic variance or covariance. f_{ST} = inbreeding coefficient.

TABLE 3

χ^2 -values for testing the significance of individual values of f_{ST}

Area	D.F.	χ^2		
		p	q	
Kagoshima	15	41.7***	35.9**	43.8***
Tokushima	13	17.4	71.1***	32.7**
Kami-ina	5	19.8**	3.8	25.7***
Chiisagata	8	7.0	2.4	7.9
Sado	6	27.2***	9.7	22.7***
Tsushima	11	38.6***	49.2***	37.1***
Oki	4	6.0	29.9***	11.4*
Kuroshima	7	22.4**	31.8***	27.0***

* Significant at the 5 per cent. level.

** Significant at the 1 per cent. level.

*** Significant at the 0.1 per cent. level.

The randomness of differentiation of gene frequencies can be tested by comparing the observed with the expected correlations of gene frequencies (Nei, 1965). The expected and observed correlations, obtained by the method given by Nei and Imaizumi (1966a), are presented in table 4. In this table the "direct" and "corrected"

observed correlations refer to the correlation coefficients obtained from the "total" and "genetic" variances and covariances respectively. It is seen that the observed correlations in Kagoshima Prefecture are in good agreement with the expected, while in Tokushima Prefecture they deviate considerably from these. This again suggests that the differentiation in the latter Prefecture has not occurred at random or the locations of blood group typing were not chosen at random.

TABLE 4
Correlations between different gene frequencies in Kagoshima and Tokushima Prefectures

Gene frequencies concerned	Kagoshima			Tokushima		
	Expected	Observed		Expected	Observed	
		Direct	Corrected		Direct	Corrected
$p \cdot q$	-0.266	-0.145	-0.086	-0.291	-0.341	-0.613
$p \cdot r$	-0.739	-0.806	-0.829	-0.717	-0.327	0.338
$q \cdot r$	-0.453	-0.458	-0.469	-0.459	-0.777	-0.951

3. DIFFERENTIATION WITHIN AREAS SMALLER THAN PREFECTURES

There are several data with which the local differentiation of gene frequencies within areas smaller than Prefectures can be studied. Two of them refer to inland districts, which are smaller in size than Prefecture but larger than *mura* or *machi*. The two districts employed here are Kami-ina and Chiisagata, both of which are located in Nagano Prefecture (*cf.* Nei and Imaizumi, 1966*a*). The former consists of 6 *mura* and the latter of 9 *mura*, their total populations in 1950 being 18,140 and 37,261 respectively. The data on the ABO blood group frequencies in these districts have been obtained by Hukuda *et al.* (1954) and Tanaka *et al.* (1957).

Other data refer to small islands surrounding the mainlands of Japan, *i.e.* Sado, Tsushima, Oki (one of the two islands, *i.e.* Togo), and Kuroshima Islands. The data on these islands were once utilised for the study of the differentiation of gene frequencies among isolated populations (Nei and Imaizumi, 1966*b*). The areas of the above islands are 829 km², 703 km², 244 km², and 4.6 km² respectively, and the population sizes at the 1960 census are 84,397, 69,551, 26,846, and 2,262, respectively. In each of the islands the blood group frequencies have been determined at several locations. In 1950 Sado Island comprised 25 *mura* or *machi*, of which seven were chosen for blood group typing, whereas, in Togo Island of Oki, four *mura* were chosen out of the

eight (Kobayashi and Katoh, 1957; Kobayashi *et al.*, 1957). In Kuroshima (a *machi*) all *buraku*, smallest administrative units of Japan, were subjected to blood group typing (Schull *et al.*, 1962). In Tsushima the locations appear to have been chosen almost at random (Kobayashi, 1952).

Tables 5 and 6 show the blood group frequencies and gene frequency estimates obtained by Bernstein's method. The χ^2 for testing

TABLE 5

ABO blood group frequencies and estimates of gene frequencies in inland small districts

(i) Kami-ina

Sub-population	N_s	N	Blood group frequency				Gene frequency			χ^2
			<i>O</i>	<i>A</i>	<i>B</i>	<i>AB</i>	<i>p</i>	<i>q</i>	<i>r</i>	
Takato	910	4,469	34.6	30.8	25.2	9.4	0.226	0.191	0.583	1.1
Kanami	457	2,254	31.1	33.9	27.1	7.9	0.238	0.195	0.567	1.6
Nagafuji	524	2,569	29.0	33.6	28.1	9.3	0.245	0.210	0.545	0.8
Fujisawa	374	3,033	25.7	38.2	26.5	9.6	0.280	0.202	0.518	1.7
Miwa	500	3,191	22.6	39.2	26.8	11.4	0.299	0.215	0.486	1.6
Inasato	397	2,624	24.9	36.8	29.5	8.8	0.266	0.217	0.517	4.5
Total*	3,162	18,140	29.0	34.7	26.9	9.4	0.254	0.203	0.543	3.5
(ii) Chiisagata										
Kawabe	82	3,717	22.0	42.7	28.0	7.3	0.299	0.200	0.501	2.8
Nakashioda	202	5,685	32.7	33.6	22.3	11.4	0.257	0.184	0.559	1.3
Higashishioda	1,866	5,717	29.4	35.6	24.0	11.0	0.269	0.193	0.538	1.2
Nishishioda	1,120	4,201	29.3	34.4	25.5	10.8	0.259	0.202	0.539	0.2
Betsusho	49	2,242	22.4	38.8	34.7	4.1	0.252	0.225	0.523	4.2
Izumida	42	3,298	28.6	30.9	23.8	16.7	0.271	0.224	0.505	1.2
Urasato	665	4,430	27.5	36.5	23.5	12.5	0.284	0.199	0.517	1.4
Muroga	90	2,364	20.0	41.1	27.8	11.1	0.313	0.221	0.466	0.9
Aoki	2,460	5,607	27.4	37.0	24.0	11.6	0.283	0.197	0.520	0.8
Total*	6,576	37,261	28.3	36.1	24.3	11.3	0.275	0.197	0.528	2.3

* Gene frequencies in the row of "Total" refer to the weighted mean. N_s = sample size. N = population size in 1950.

the departure from the Hardy-Weinberg equilibrium is significant at the 5 per cent level in 5 of the 47 sub-populations in total. χ^2 -test also indicated that the heterogeneity of gene frequencies among sub-populations is statistically significant in all areas except Chiisagata District.

The average values of the estimates of f_{ST} obtained from different gene frequencies and gene frequency combinations are given in table 7. It can be seen that the degree of differentiation is quite high for all

TABLE 6

ABO blood group frequencies and estimates of gene frequencies in small islands

(i) Sado

Sub-population	N_s	N	Blood group frequency				Gene frequency			χ^2
			<i>O</i>	<i>A</i>	<i>B</i>	<i>AB</i>	<i>p</i>	<i>q</i>	<i>r</i>	
Ryotsu	560	9,402	31.4	33.8	25.9	8.9	0.243	0.193	0.564	0.1
Kamo	193	7,223	39.4	33.2	21.2	6.2	0.222	0.148	0.630	0.1
Aikawa	684	8,509	31.6	36.7	22.6	9.1	0.264	0.174	0.562	0.0
Kawasaki	70	6,086	28.6	30.0	24.3	17.1	0.267	0.230	0.503	1.4
Suizu	177	1,802	28.8	39.0	26.0	6.2	0.263	0.179	0.558	3.3
Iwakubi	162	1,728	19.1	51.2	21.0	8.7	0.373	0.164	0.463	3.4
Matsugasaki	137	2,011	27.0	35.8	29.2	8.0	0.253	0.210	0.537	1.5
Total*	1,983	36,761	30.6	36.6	24.1	8.7	0.262	0.181	0.557	2.0
(ii) Tsushima										
Toyosaki (1)	276		35.1	44.6	12.3	8.0	0.309	0.107	0.584	1.3
Toyosaki (2)	61		23.0	47.5	9.8	19.7	0.413	0.155	0.432	4.2
Sasuna	391		29.4	39.6	21.5	9.5	0.287	0.169	0.544	0.0
Nita (1)	197		32.5	34.0	26.9	6.6	0.231	0.186	0.583	1.5
Nita (2)	244		34.0	35.3	20.5	10.2	0.260	0.167	0.573	1.1
Nita (3)	356		29.5	39.9	21.6	9.0	0.286	0.167	0.547	0.2
Mine (1)	104		23.1	33.6	32.7	10.6	0.256	0.249	0.495	0.7
Mine (2)	101		29.7	36.6	20.8	12.9	0.286	0.184	0.530	0.9
Sasu	119		29.4	41.2	24.4	5.0	0.271	0.162	0.567	3.2
Tsutsu	502		40.0	36.7	16.1	7.2	0.249	0.124	0.627	1.2
Hisada (1)	60		35.0	13.4	33.3	18.3	0.168	0.294	0.538	7.0
Hisada (2)	128		44.5	25.8	25.0	4.7	0.166	0.162	0.672	0.2
Total*	2,539		33.3	37.4	20.5	8.8	0.267	0.160	0.573	0.6
(iii) Oki										
Goka (1)	240		31.2	34.2	25.0	9.6	0.250	0.191	0.559	0.0
Goka (2)	52		38.5	28.8	25.0	7.7	0.203	0.179	0.618	0.0
Saigo	93		21.5	24.7	39.8	14.0	0.217	0.320	0.463	0.0
Fuse	155		41.3	31.0	18.0	9.7	0.227	0.148	0.625	3.0
Naka	429		32.2	40.3	19.8	7.7	0.280	0.149	0.571	0.3
Total*	969		32.7	35.2	23.0	9.1	0.254	0.177	0.569	0.1
(iv) Kuroshima										
Motomura	45	218	24.5	60.0	11.1	4.4	0.408	0.082	0.510	0.6
Furusato	52	245	50.0	26.9	15.4	7.7	0.189	0.122	0.689	1.5
Todobira	48	270	31.3	39.6	20.8	8.3	0.279	0.159	0.562	0.0
Hikazu	39	185	28.2	30.8	7.7	33.3	0.368	0.213	0.419	13.3
Tashiro	88	342	22.7	28.4	36.4	12.5	0.232	0.286	0.482	0.1
Warabi	68	298	11.8	32.3	39.7	16.2	0.288	0.342	0.370	1.0
Neya	69	282	17.4	46.4	14.5	21.7	0.424	0.196	0.380	2.2
Nakiri	99	422	23.2	40.4	19.2	17.2	0.343	0.199	0.458	1.7
Total*	508	2,262	24.8	37.6	22.4	15.2	0.313	0.212	0.475	3.7

* Gene frequencies in the row of "Total" refer to the weighted means. N_s = sample size. N = population size.

populations except Chiisagata, where the f_{ST} is negative but not significant, as indicated by the χ^2 -test for the heterogeneity of gene frequencies (see also table 3). The value for Kuroshima is 30 times higher than that for the whole of Japan. It is also worthy of noting that the degree of differentiation is negatively correlated with $\bar{N}_s$, the average sample size of sub-population. The standard deviation of observed value of f_{ST} was computed in order to know the heterogeneity of f_{ST} . This standard deviation (s_f) indicates that the heterogeneity of f_{ST} is considerably high for Kuroshima and Oki populations. Note that this standard deviation cannot be used for testing the statistical significance of f_{ST} , since the six observed values of f_{ST} from which s_f has been obtained are not fully independent.

TABLE 7

Degrees of differentiation of gene frequencies and other parameters in areas smaller than Prefectures

Area	No. of sub-populations	$\bar{N}_s$	$\bar{f}_{ST}$	s_f
Kami-ina	6	570.0	0.0013	0.0037
Chiisagata	9	730.7	-0.0005	0.0004
Sado	7	283.3	0.0028	0.0025
Tsushima	12	211.6	0.0070	0.0016
Oki	5	193.8	0.0073	0.0079
Kuroshima	8	63.5	0.0225	0.0068

$\bar{N}_s$ = average sample size of sub-population.

$\bar{f}_{ST}$ = mean degree of differentiation.

s_f = standard deviation of observed value of f_{ST} .

The χ^2 -values for testing the significance of individual values of f_{ST} are given in table 3. In Tsushima and Kuroshima all of the three gene frequencies are almost equally differentiated. In other areas, on the other hand, only two show a significant differentiation (excepting Chiisagata).

The expected and observed correlations between different gene frequencies are set out in table 8. In Tsushima and Kuroshima the observed correlation is in good agreement with the expected for all combinations of gene frequencies. In the other three areas, however, the agreement between the expected and observed correlations is not good. This disagreement appears to be partly due to sampling error because of the small number of sub-populations employed but mainly due to the fact that only two gene frequencies are significantly differentiated among sub-populations. In Kami-ina and Sado the frequency of I^B or q shows no significant differentiation, so that the correlation between p and q or q and r has little meaning, whereas, in Oki, the correlation between p and q or p and r is meaningless for the same reason. The remaining correlations are then expected to become

negatively high (up to -1), since the differentiation has occurred as if there were only two alleles. Table 8 shows that this is actually the case.

TABLE 8

Correlations between different gene frequencies in areas smaller than Prefecture

Gene frequencies concerned	Expected	Observed		Expected	Observed	
		Direct	Corrected		Direct	Corrected
		Kami-ina			Tsushima	
$p \cdot q$	-0.295	0.776	$-*$	-0.263	-0.327	-0.366
$p \cdot r$	-0.636	-0.982	-1.104	-0.699	-0.638	-0.597
$q \cdot r$	-0.550	-0.881	$-*$	-0.506	-0.520	-0.528
		Sado			Kuroshima	
$p \cdot q$	-0.280	-0.161	-0.125	-0.350	-0.268	-0.261
$p \cdot r$	-0.668	-0.878	-0.952	-0.642	-0.599	-0.562
$q \cdot r$	-0.527	-0.332	-0.184	-0.493	-0.611	-0.652
		Oki				
$p \cdot q$	-0.271	-0.555	-1.253			
$p \cdot r$	-0.670	0.037	1.490			
$q \cdot r$	-0.533	-0.852	-1.033			

* The estimate of genetic variance turned out to be negative, so that the corrected correlation could not be obtained.

4. DISCUSSION

The present investigation has shown that the *ABO* blood group gene frequencies are locally differentiated in all but one of the eight areas examined. Theoretically, it may be expected that the degree of the differentiation becomes high as the geographical area involved increases. In practice, however, the estimate of f_{ST} has shown a rather reverse tendency. Namely, the estimate of f_{ST} for Prefecture was larger than that for the whole of Japan, and the estimate for areas smaller than Prefecture was larger than that for Prefecture on the average. This paradoxical tendency has arisen mainly by the fact that the unit of sub-population was not the same for all levels of geographical areas. In the case of the whole of Japan the unit of sub-population was Prefecture, while in the analysis of local differentiation within Prefecture it was *mura*, *machi* or city. In the case of the areas smaller than Prefecture the unit was *buraku* or *machi*, though not clearly described in some of the original papers from which the data were taken. The

exact size of neighbourhood in Wright's (1946) sense is not known at present. Schull *et al.* (1962) examined the marriage pattern in Kuroshima and found that endogamy within *buraku* is rather a rule. Thus, in this Island each *buraku* represents a neighbourhood approximately (usually ten to twenty *buraku* constitute a *mura* or *machi*), though this may be exceptional since Kuroshima is a small island. In other areas the size of neighbourhood appears much larger than *buraku* but not larger than *mura* at least in the past. Thus, if the unit of sub-population is enlarged, it is likely to include many neighbourhoods. A Prefecture, for example, certainly includes a large number of neighbourhoods. Therefore, the value of f_{ST} based on a large unit of sub-population is expected to become small, provided that the differentiation has occurred at random.

In Wright's theory the size of neighbourhood is defined in relation to geographical distribution. In human populations, however, marriages are contracted not only for geographical but also for social and economical reasons. The latter reasons are particularly important in large cities, where migration involves small distances and social and economical gradations are more variable than in rural areas. It is, therefore, meaningless to apply Wright's theory to a large city population as done by Spuhler (1961). In rural areas such as the populations employed in the present investigation, however, the relative importance of geographical factor is considered to be large, and thus the concept of neighbourhood is still useful.

Nei and Imaizumi (1966a, b) have shown that the local differentiation of *ABO* blood group gene frequencies in Japan has occurred largely at random. On the other hand, the present investigation revealed that the differentiation within small areas is not necessarily at random. This non-random differentiation may be due to either inadequate sampling of locations for blood group typing or local variation in selection intensity or both. In practice, however, the latter factor does not appear very important, since its effect must be so small that the differentiation in the whole of Japan becomes nearly at random. The selection for *ABO* blood groups, if any, would show a random local variation, though in a slight degree.

5. SUMMARY

The local differentiation of *ABO* blood group gene frequencies in two Prefectures and six areas smaller than Prefectures in Japan was studied. The degree of differentiation among sub-populations within Prefectures was smaller than that within areas smaller than Prefectures on the average. This paradoxical result was ascribed to a smaller unit of sub-population employed in the latter. When *buraku*, smallest administrative unit of Japan, was used as a unit of sub-population, the differentiation as measured by inbreeding coefficient was as high as

2 per cent. in a small area (an island). An analysis of the correlation between different gene frequencies showed that the differentiation of gene frequencies is not at random in four of the eight areas examined.

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