On the relationship between the number of spermatozoa and the probability of conception

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Summary. A simple model is proposed to relate spermatozoan numbers to the proba-
bility of conception, based on the Poisson distribution. It is compared with van Duijn's (1964)
model. Both models are fitted to several series of data taken from the literature and either
model gives a satisfactory fit. The Poisson model may be preferred because it is easier to
apply and has a simpler biological interpretation.

Introduction.

The probability P of conception following coitus or insemination is a function of
the number, or concentration, of spermatozoa. Let N be the number, or the concentra-
tion in a given volume. Curves observed in numerous examples of data on artificial
insemination in animals show that P rises sharply with N, then flattens out towards a
plateau (Salisbury and van Demark, 1961). To represent this curve, van Duijn (1964)
proposed a general equation of fertility based on certain considerations of sperm kine-
tics. A simplified form of the expression is

$$P = P_\infty [1 - e^{-k \log_e(N/N_i)}] , \qquad N \geqslant N_i , \qquad (1)$$

where P_∞ is the maximum that P can attain, k is a constant and N_i is a threshold value
below which the probability of conception is zero. This model fits the data presented by
the author remarkably well. Nevertheless, we have reservations about the hypotheses
on which the model is based. It introduces, for example, assumptions about aspects of
sperm kinetics which are in reality very complicated and not well understood. In conse-
quence, we have been motivated to look for an alternative model with a simpler and less
controversial biological explanation.

Such a model is proposed in this paper. Using different series of animal data, the
model is compared to that of van Duijn (1964) with respect to the goodness of fit and
with respect to how much is learned biologically by fitting the model.

The model proposed.

The probability of conception is written :

$$P = P_0 P_f P_v ,   (2)$$

where P_0, P_f and P_v are, respectively, the probabilities that a fertilizable ovule is pro-
duced, that it is fertilized and that the egg so formed is viable. P_f is assumed to be given
by the following model : each of the N spermatozoa inseminated has, independently,
the same probability P_e of being efficacious, that is to say, capable of fertilizing the
ovule if the ovule has not already been fertilized by another spermatozoon. Since N is
very large, it follows that the number of efficacious spermatozoa follows a Poisson dis-
tribution with mean $m = NP_e$. Thus the probability that none are efficacious is e^{-m}
and, in consequence,

$$P_f = 1 - e^{-m} .   (3)$$

Setting $P_0 P_v = P_\infty$, the maximum probability attainable as N increases without limit,
(2) can be written

$$P = P_\infty (1 - e^{-NP_e}) .   (4)$$

This expression for the probability of conception will be called the « Poisson Model ».

The Poisson Model is derived on the assumption that at most one egg is available
for fertilization. It will still apply in the case of multiple eggs or repeated ovulation and
give the probability of at least one viable fertilized egg. P_e, however, will then depend
upon the number of eggs available if ovulation occurs and this number will have to be
assumed to be a constant if the model is to be fitted to data from a series of insemina-
tions.

In the case of artificial insemination, P_e will depend upon the handling and storage
of the sperm as well as the technique of insemination.

Material and methods.

Material. — The data used are experimental results from artificial insemination,
published by various authors. The references cited should be consulted for more com-
plete details of the techniques used.

1. *Cattle.*

(a) The results of Willett and Larson (1952) : 72 336 inseminations over 9 different
doses. N is expressed as the total number of spermatozoa, living and dead, per dose.
Fresh sperm was diluted in a medium containing an antibiotic, egg yolk and citrate.

(b) The same publication : 10 745 inseminations over 10 different doses.

(c) Florin (1977) : 9 214 inseminations over 4 different doses. The data are tabulat-
ed for 5 different bulls, and are ajusted for geographic region, inseminator, date of
insemination and receptor herd. N is expressed as the total number of spermatozoa
per dose. The sperm was conditioned and frozen in fine straws (0.23 ml).

(d) Branton, Kellgren and Patrick (1953) : 8356 inseminations over 7 doses. N is
expressed as the number of motile spermatozoa per ml. Fresh sperm was diluted in a
medium containing an antibiotic, egg yolk and citrate.

2. *Merino sheep.* — Data of Salamon (1962) : 6 different doses, each inseminated 50 times. N is expressed as the number of normal spermatozoa. Fresh sperm was diluted and given in doses of 0.1 ml. Vasectomised males were used to detect the oestrus of the ewes.

3. *Domestic fowl.* — Data of Taneja and Gowe (1962) : 15 different doses, each inseminated 36 times (3 different strains × 12 chickens per strain, at each dose). N is expressed as the total number per dose. The dose was varied by varying the volume of fresh undiluted sperm.

In general, the various authors have not specified the exact timing of insemination relative to the ovulatory cycle of the female. In the case of the cattle and sheep, it should be safe to assume that standard insemination techniques were used and that the timing of the dose was as close as possible to what is known to be the optimal time. The situation with chickens is quite different, where ovulation may occur daily while the sperm from one insemination can continue to fertilize eggs for as long as two or three weeks. The timing of the dose is then much less critical a factor.

Series 1a, 1b, 1d and 3 were used by van Duijn to test his model, series 1c and 2 were added for the present study. As in van Duijn (1964), P and P_∞ are expressed as the percentage of « non-returns » (that is, the percentage of successful inseminations) for the cattle and sheep. There is a difference in the domestic fowl data, in that van Duijn used the duration of fertility, measured in days from insemination, while the present study, in keeping with the interpretation of the Poisson model, uses the percentage of chickens to lay at least one fertilized egg.

Method. — The parameters of the model were estimated by the method of minimum χ^2 using the Nelder and Mead direct-search method (O'Neill, 1971 ; Hill, 1978). The minimized χ^2 value was used to test the goodness of fit.

Results and discussion.

Table I compares the fitted van Duijn model and the fitted Poisson model with the observed data. This comparison is illustrated graphically in figure 1 for Series 1a, witch had the largest number of inseminations. Table II shows the fitted parameter valuee and the goodness-of-fit tests. Inasmuch as the test statistics are only approximately χ^2 distributed, in large samples, the tests should not be regarded as rigorous criteria for accepting or rejecting the models. Rather, they are useful for indicating in a general sense the relative merits of the two models.

The fit of the van Duijn model is acceptable at the 5 p. 100 level of significance in all but 2 of the 10 series (specifically, Series 1b and Bull 5 of Series 1c). The Poisson model shows a significant departure from the data for four of the series, including the two just mentioned, but, as can be seen in table 1, these two series are somewhat abnormal with respect to relative fecundability at high concentrations. For the other two series the number of inseminations is very large and this can lead to statistically significant departures from the model even when the disparity between observed and expected is, for all practical purposes, very small : this is clearly the case in figure 1. Thus, on the whole, we conclude that the Poisson model can be considered to fit the data acceptably well.
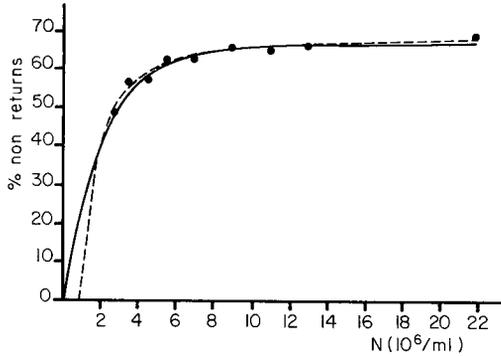
TABLE 1

Observed and predicted percentage success as a function of the number of spermatozoa.
N is expressed in 10⁶/ml. The numbers of inseminations are given in parentheses

1. Cattle

Serie Ia (Willett and Larson, 1952)

N	2.4-2.9 (732)	3.0-3.9 (2 335)	4.0-4.9 (5 365)	5.0-5.9 (5 613)	6.0-7.9 (18 846).	8.0-9.9 (12 657)	10.0-11.9 (10 593)	12.0-13.9 (9 572)	14.0-31.2 (6 623)
p. 100 observed	49.0	57.8	58.6	62.5	63.6	65.8	66.0	66.6	67.9
Van Duijn model	50.3	56.1	59.6	61.8	63.8	65.3	66.3	66.9	67.4
Poisson model	48.2	54.8	59.3	62.1	64.4	65.7	66.2	66.4	66.4

Series 1b (Willett and Larson, 1952)

N	1.5-1.9 (226)	2.0-2.9 (960)	3.0-3.9 (1 857)	4.0-4.9 (1 526)	5.0-5.9 (928)	6.0-7.9 (1 239)	8.0-9.9 (1 271)	10.0-11.9 (1 038)	12.0-13.9 (815)	14.0-21.7 (885)
p. 100 observed	52.7	55.6	59.6	63.6	63.3	63.8	65.1	70.0	72.3	68.2
Van Duijn model	50.3	56.4	60.2	62.3	63.7	65.1	66.2	66.9	67.5	68.2
Poisson model	44.6	53.9	60.5	64.1	66.0	67.3	67.9	68.1	68.1	68.1

Series 1c (Florin, 1977)

	Bull 1				Bull 2				Bull 3				Bull 4				Bull 5			
N	6 (390)	12 (475)	16 (442)	25 (476)	6 (286)	12 (332)	16 (317)	25 (351)	6 (413)	12 (500)	16 (492)	25 (556)	6 (449)	12 (517)	16 (535)	25 (522)	6 (489)	12 (558)	16 (509)	25 (605)
p. 100 observed	45.3	56.8	62.1	67.4	44.7	52.3	55.6	58.3	55.8	60.3	63.2	63.5	61.6	65.1	66.5	67.0	56.6	61.4	69.8	69.2
Van Duijn model	45.1	57.4	61.6	67.4	44.6	52.6	55.2	58.4	55.7	60.9	62.3	63.8	61.5	65.3	66.2	67.1	56.2	63.8	66.5	69.9
Poisson model	43.5	58.7	62.8	66.1	43.7	54.0	55.9	57.1	55.3	61.9	62.6	62.8	61.4	66.0	66.3	66.4	56.6	65.7	67.4	68.2

Series 1d (Branton, Kellgren and Patrick, 1953)

N	4.0-5.9 (463)	6.0-7.9 (1 557)	8.0-9.9 (1 697)	10.0-11.9 (1 274)	12.0-13.9 (911)	14.0-15.9 (1 198)	16.0-33.4 (1 256)
p. 100 observed	59.8	62.7	62.2	62.9	64.1	64.2	70.5
Van Duijn model	59.0	61.2	62.8	64.0	65.0	65.0	68.5
Poisson model	57.4	62.0	64.0	64.8	65.2	65.2	65.5

TABLE 1 *(end)*

2. Sheep

Salamon, (1962)

N	49.6 (50)	52.8 (50)	62.9 (50)	69.2 (50)	76.6 (50)	83.2 (50)
p. 100 observed	44	40	56	50	60	64
Van Duijn model	41.1	44.1	51.9	55.6	59.3	62.1
Poisson model	43.3	45.3	51.3	54.7	58.4	61.4

3. Domestic fowl

Taneja and Gowe, (1962)

N	1.3 (36)	3.9 (36)	6.5 (36)	13.2 (36)	19.7 (36)	26.3 (36)	32.9 (36)	39.5 (36)
p. 100 observed	11.1	61.1	63.9	72.2	88.8	94.4	97.2	94.4
Van Duijn model	9.7	60.7	73.3	84.4	88.5	90.7	92.2	93.2
Poisson model	15.7	39.9	57.0	81.3	91.1	95.2	96.9	97.6

N	46.1 (36)	65.8 (36)	131.1 (36)	197.4 (36)	329.0 (36)	658.0 (36)	987.0 (36)
p. 100 observed	97.4	100.0	100.0	100.0	100.0	100.0	100.0
Van Duijn model	94.0	95.4	97.3	98.0	98.6	99.2	99.4
Poisson model	97.9	98.1	98.1	98.1	98.1	98.1	98.1

FIG. 1. — *Percentage of non-returns as a function of the concentration of spermatozoa at the doses insemi-nated. Series of Willett and Larson (1952).* —— *Poisson model ; - - - van Duijn model ;* ● *observed point.*

TABLE 2

Parameter estimates and goodness-of-fit tests

Series	Number of inseminations	Parameter estimates					Goodness of fit : significance level for χ^2 test	
		Van Duijn			Poisson		Van Duijn	Poisson
		P_∞	k	N_i ($\times 10^6$)	P_∞	P_e ($\times 10^{-6}$)		
1a	72 336	69.9	1.2	0.9	66.5	0.5	0.13	0.002
1b	10 745	70.5	0.9	0.5	68.0	0.6	0.02	0.001
1c B_1	1 783	100.0	0.4	1.2	66.9	0.2	0.75	0.45
B_2	1 286	70.6	0.5	0.9	57.2	0.2	0.85	0.70
B_3	1 961	66.6	0.9	0.9	62.8	0.3	0.60	0.75
B_4	2 023	68.4	1.2	0.8	66.4	0.4	0.85	0.85
B_5	2 161	87.9	0.4	0.5	68.3	0.3	0.04	0.04
1d	8 356	100.0	0.2	0.02	65.8	0.4	0.15	0.04
2	300	100.0	0.9	28.6	100.0	0.01	0.75	0.85
3	540	100.0	0.76	1.14	98.3	0.13	0.37	0.24

The goodness-of-fit tests in table 2 might lead one to think that the van Duijn model performs better than the Poisson model for these series of data, but this conclusion is not without reservations. The van Duijn model has 3 parameters, while the Poisson model has only 2. The extra flexibility of the van Duijn model can thus lead to appa-rently better fits, but not necessarily in a biologically meaningful way. For example, in 4 of the series the best fit was obtained with $P_\infty = 100$ p. 100. In fact, the fit was even

closer when P_∞ was allowed to exceed 100 p. 100, which would be meaningless bio-logically. Thus the values of P_∞ estimated by the van Duijn model are less credible bio-logically than those estimated by the Poisson model *. Furthermore, in the van Duijn model the probability of fertilization is zero below a minimum value of N, which is about 1 million/ml in Series 1a. This comes from one of van Duijn's hypotheses, concern-ing the exponential decrease in the number of spermatozoa able to fertilize, between the moment of insemination and the moment of fertilization. In none of the series studied are there points obtained for low concentrations and low probabilities, so there is no evidence either for or against the existence of such a threshold. In any event, relati-vely good rates of success have been reported in cattle with concentrations well below 1 million/ml (Kim and Lee, 1972 ; Shannon, 1972 ; Jondet, 1973).

There are two further advantages to the Poisson model. First of all, the underlying explanation is entirely logical. Insemination introduces a very large number of sper-matozoa, each one of which has a very small chance of being « efficacious », and these are exactly the conditions that lead to the Poisson distribution. Admittedly, the sperma-tozoa must also be assumed to be statistically independent of each other and this would not be the case if some minimum number of efficacious spermatozoa were necessary to fertilize an egg. A model based on this hypothesis was tested on the same series of data and invariably gave a poorer fit than the Poisson model. Another assumption implicit in our model is that P_e is independent of N. This is the simplest version of the Poisson model. One could perhaps envisage a case where P_e decreases as N increases, so that the mean number of efficacious spermatozoa $m = NP_e$ increases less than proportio-nally to N. Assuming that m increases as log N (or, more precisely, as log N/N_i) leads to the van Duijn model. Alternatively, assuming that m cannot exceed some maximum value, and increases as $1 - e^{-\lambda N}$, leads to the Gompertz law. The Gompertz model, and other extensions of the Poisson model, have all been tested of the same series of data but give no appreciable improvement in the fit in return for the loss of simplicity.

The simplicity of the Poisson model is its other advantage. The equation $P = P_\infty(1 - e^{-m})$ expresses the chance of conception as a product of two terms : $1 - e^{-m}$, which concerns fertilization, and $P_\infty = P_0 P_v$, which concerns the events before and after that moment. The value of P_∞ is of great theoretical interest as an estimate of the rate of lost eggs and lost ovules, even though the factors due to eggs and ovules cannot be estimated separately. Thus, in the cattle series studied, P_∞ is estimated to be in the range of 60 to 70 p. 100, so the rate of loss of ovules or eggs is about 30 to 40 p. 100. As for the term P_f, its expression by the equation $P_f = 1 - e^{-m}$ where $m = NP_e$ is interesting for both theoretical and practical reasons. Theoretically, we observe that, in cattle, less than 1 spermatozoon per million (from 0.2 to 0.7) is « efficacious ». Practically, this equation expresses the dose-effect relationship. Noting that, for example, $m = NP_e = 5$ gives $e^{-m} = 0.007$, or $P_f = 99.3$ p. 100, which is virtually 100 p. 100, an increase in dose beyond that level would be useless. This can be verified in Series 1a where $m = 5$ corresponds to the dose $N = 5/P_e = 10$ millions/ml.

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* The present study is based on the values of P_∞ obtained by our method which optimizes the fit of the model to the data. Van Duijn obtained lower values of P_∞ by a graphical method, but using his estimates of the 3 parameters gives a poorer fit by the χ^2 criterion.

Choosing m = 4 reduces P_f to 98.2 p. 100, which is only 1.2 p. 100 less than the previous case although the dose has been reduced by 20 p. 100. By working along these lines, cost-effectiveness can be optimized. The equation of the Poisson model can be used for this purpose as it gives an excellent approximation in the range of concentrations which are of practical interest.

It is possible to envisage the application of the Poisson model to human reproduction. Even though the concentration of sperm varies markedly from one ejaculation to another by the same subject (Schwartz *et al.*, 1979) one can assign an average value of N to each man. While the variation in N from one man to another is not, of course, the same as variation in dose by dilution, the two problems are evidently very similar. The animal data suggest that variation in male fertility as a function of N should be considered from a probabilistic point of view ; the probability should increase at first and then level off for a sufficiently large value of N. This is indeed what has been observed in several epidemiological studies which have been carried out (David *et al.*, 1979 ; David *et al.*, 1980). One complication for human reproduction is the possibility of intercourse several times in the same menstrual cycle, which leads to some manner of accumulation of spermatozoa. A simple hypothesis is that the probabilities of fertilization from acts of intercourse on different occasions are statistically independent. If we denote by $P_{f,i}$, $P_{f,j}$ and $P_{f,ij}$ the probabilities of fertilization for intercourse on day i only, day j only and the two days i and j, respectively (assuming intercourse at most once per day), then

$$1 - P_{f,ij} = (1 - P_{f,i}) (1 - P_{f,j}) .$$

Such an hypothesis has been tested on reliable data and found to give encouraging results (Schwartz, Macdonald and Heuchel, 1980). Assuming the Poisson model, it follows that $P_{f,i} = 1 - e^{-m_i}$ and hence that $P_{f,ij} = 1 - e^{-(m_i + m_j)}$, thus the probability of fertilization depends upon the sum of the numbers of efficacious spermatozoa from the two acts of intercourse. Note, however, that in this case the probability P_e of being efficacious will vary from day to day, depending upon the timing of intercourse relative to ovulation. This result can be extended to coitus on more than two occasions and is yet another advantage of the Poisson model.

To summarize, the Poisson model provides a convenient and interesting approximation over the medium range of concentrations. It is, evidently, only one of many possible approaches to the problem but, because of its simplicity and ease of utilization, we have chosen to retain it in favour of other models, such as that of van Duijn, which fit the data about as well.

Conclusion.

Insofar as the two models presented are used to describe a dose-effect relationship, where dose refers to concentration of sperm and the effect is the probability of conception, they can be applied without making any assumptions about the biological processes which control conception. In that sense, the question of compatibility between the model and the different assumptions which may be made about these processes does not arise. These processes concern the transport and survival of spermatozoa and

their eventual capacity to fertilize ; the role of crypts in the uterine wall and the possible filter and reservoir effects at different levels of the female genital tracts, through which successive fluxes of spermatozoa travel towards the site of fertilization. These different mechanisms can be taken into account in the parameters of the models but need not affect their formulation as long as they are regarded as empirically justified dose-effect relations. For example, the time between insemination and the arrival of the gametes at the site of fertilization does not appear explicitly in the Poisson model because it is integrated into the probability P_e for a spermatozoon to be efficacious, this probability being smaller the further removed insemination is from the time of ovulation.

The dose-effect relationship, under either model, is marked by a limiting factor : beneath a certain level of N, the probability of fertilization drops abruptly. Further studies would be necessary to establish whether it is simply numbers that matter, as implied by the Poisson model, or whether the nature of sperm itself is different at lower densities.

On the other hand, the few data that exist on the other characteristics of sperm, and in particular on motility after thawing (Linford et al., 1976), suggest curvilinear relationships for the probability of conception that are close to those of the present study. It would be of interest to model these relations in the hope of dissociating the qualitative and quantitative aspects of the fertilizing potential of a sperm.

Résumé. Un modèle simple, basé sur la loi de Poisson, et mettant en relation le nombre de spermatozoïdes et la probabilité de conception, est proposé dans cette étude. Il est comparé à celui de Van Duijn (1964). Les deux modèles, appliqués à plusieurs séries de données, fournissent un ajustement satisfaisant. Le modèle de Poisson apparaît plus avantageux du point de vue de la simplicité de son utilisation, et de son caractère explicatif.

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