

## Regulation of sex chromosome constitution of somatic and germ cells in the wood lemming

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**Summary.** The wood lemming displays certain peculiar features. (a) The sex ratio shows a prevalence of females, and some females produce only female offspring. (b) A considerable proportion of the females has XY sex chromosomes in the somatic tissues, but the Y is absent in the germ line. (c) Therefore, we postulate a mechanism of double non-disjunction in early embryonic life of the XY females eliminating the Y in the germ line and replacing it by duplication of the X. (d) It is assumed that the X of XY females bears a sex reversal factor ( $X^*$ ) which affects the male-determining action of the Y. (e) There is evidence that in most cases the  $X^*Y$  females are those that produce daughters only, but (f) a few exceptions may occur suggesting that regulation according to (c) and perhaps also to (d), is incomplete. Moreover, sex chromosome aberrations are not uncommon in this species. They are similarly to be attributed, at least in part, to a defect of the postulated, mechanism controlling the change of  $X^*Y$  in somatic cells to  $X^*X^*$  in germ cells. Obviously the special cytogenetic conditions of the wood lemming serve to regulate the sex ratio which, itself, probably influences or governs the dynamics of population density. It is not impossible that the situation in the wood lemming is a model of an ecological and evolutionary principle active in some other species as well.

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There is evidence to consider the wood lemming, *Myopus schisticolor* Lilljeborg, as a natural model of the potential provided by sex chromosome disparity of the somatic and germ cell compartments for the determination of sex and its role in the regulation of population dynamics.

The wood lemming is a small rodent inhabiting the mossy forests of northern Eurasia. Its distribution area in Europe covers great parts of Fennoscandia (fig. 1, according to Siivonen, 1976). Violent fluctuations in number and population bursts, not unlike those of the Norwegian or mountain lemming, *L. lemmus*, have been observed in geographically distant and unrelated areas, often with long intervals of years. Wild populations and captive stocks of the wood lemming show a

conspicuous excess of females with almost 4 times more females than males (Kalela and Oksala, 1966 ; Frank, 1966). Kalela and Oksala (1966) distinguished two types of females, based on their breeding analyses ; one produced both sons and daughters (MF-type females), and the other produced daughters only (F-type females), guaranteeing a mean sex ratio\* of about 0.25 or even less (Frank, unpublished). These authors

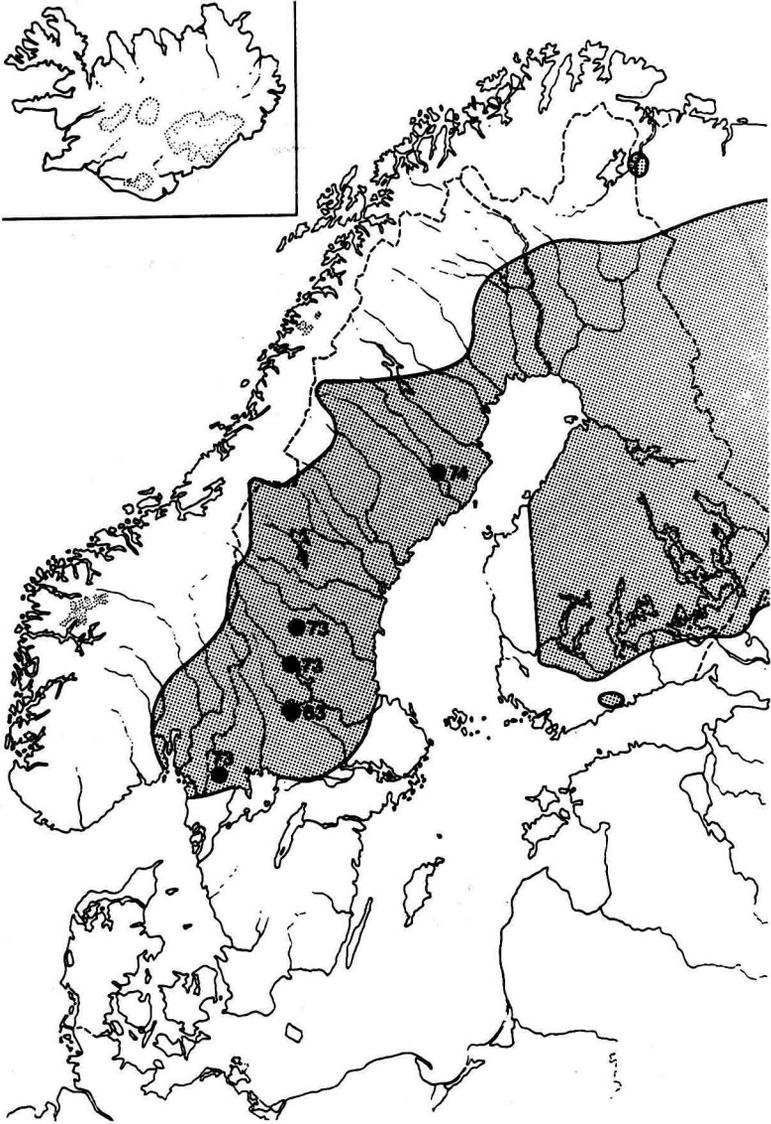


FIG. 1. — Distribution of the wood lemming in Fennoscandia (from Siivonen, 1976). Dots refer to localities and year of collection of chromosomally studied wood lemmings.

\* Sex ratio expressed as  $\frac{\text{♂}}{\text{♂} + \text{♀}}$ .

further demonstrated that whether the offspring are mixed or females only depends on the mother and not on the father, and that both types of mothers (MF and F) are able to produce both types of daughters.

We felt that any explanation of these peculiar reproductive patterns had to begin with a cytogenetic study of somatic cells and germ cells, and especially with an investigation of sex chromosomes.

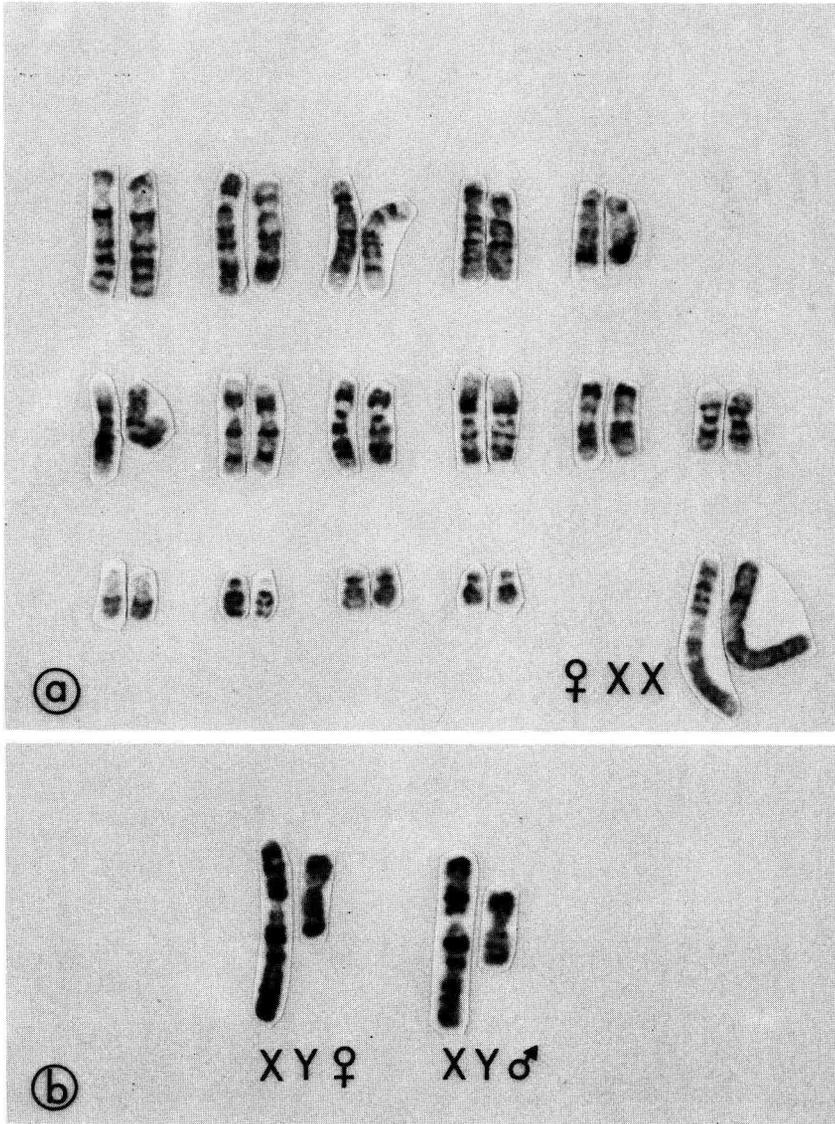


FIG. 2. — G-banded complete karyotype of an XX female (a) and sex chromosome pair from an XY female and XY male (b).

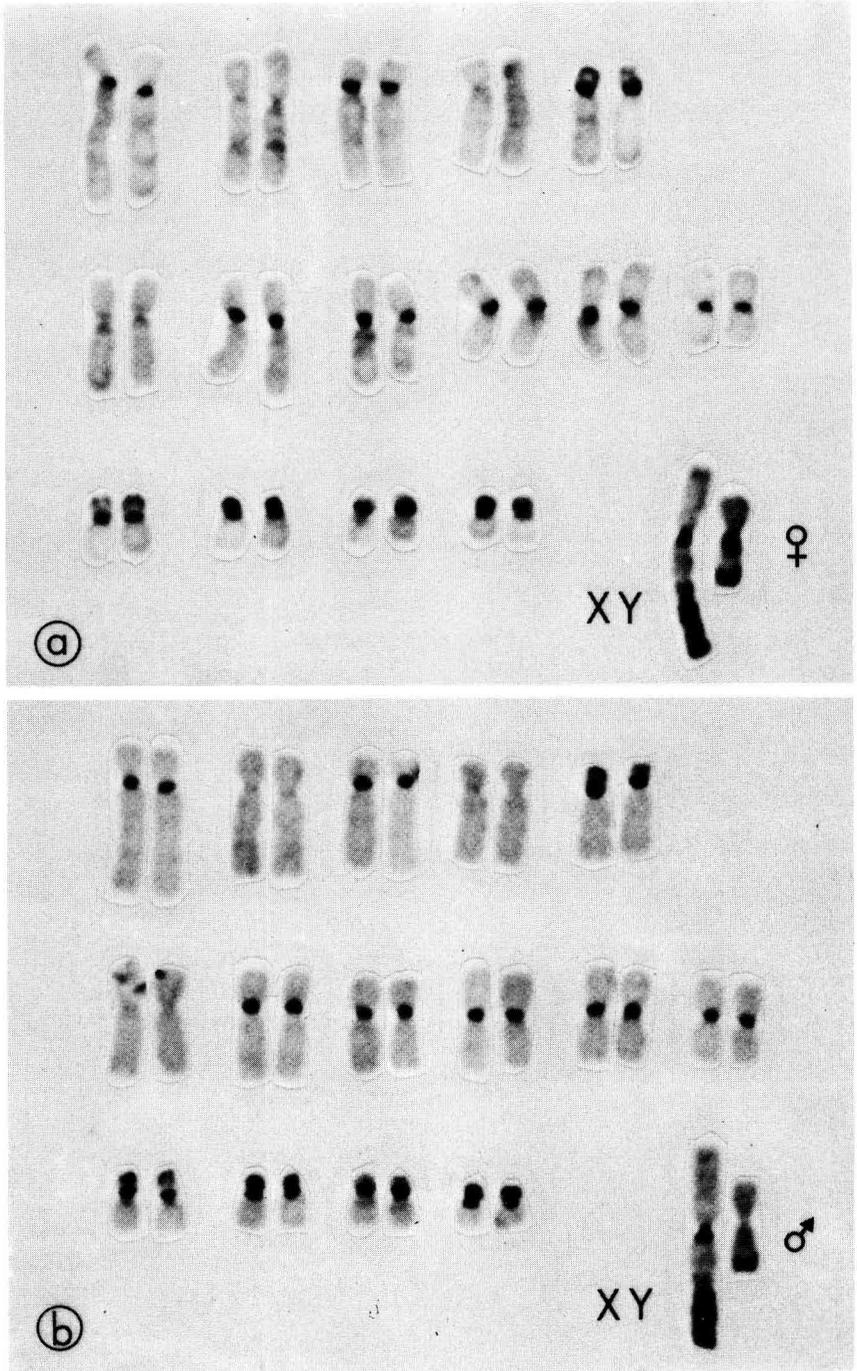


FIG. 3. — Complete C-banded karyotype of X\* Y female (a) and XY male (b).

A first cytogenetic observation revealed the existence of two different female chromosome types (Fredga *et al.*, 1976). Among the 927 females karyotyped so far from colonies bred in Braunschweig and Lübeck, 475 = 51.2 p. 100 displayed two X-chromosomes, as shown in a G-band karyotype in the upper part of figure 2. The X-chromosome, not unlike that of other *Microtinae*, is of rather large size. The remaining 452 females = 48.8 p. 100 of all females, showed an XY sex chromosome constitution with chromosomal banding patterns almost similar to those of XY males (fig. 2b). The possibility of small band differences in the short arm of these Xes is under study. The gross similarities, however, of the Xes and the Ys are underlined by a comparison of C-banded karyotypes from an XY female and an XY male (fig. 3a, b). Moreover, identity of the Ys and exclusion of any possibility of a deleted X in the case of a « female Y » is demonstrated with Q-, 33258H-banding and by a comparative study of BrdU-Giemsa replication patterns (Herbst, unpublished).

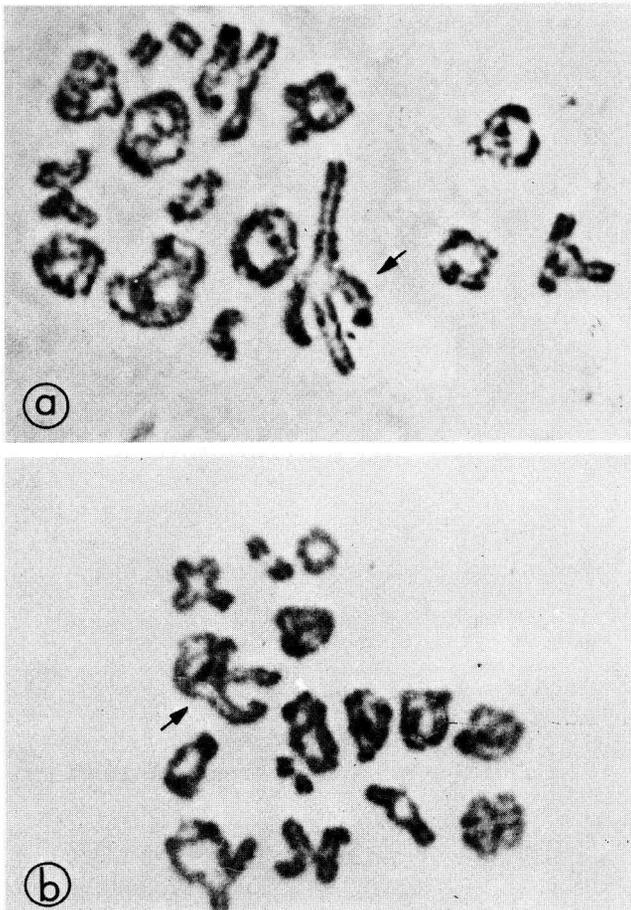


FIG. 4. — 1st meiotic metaphase (M I) of XX female (a) and X\*Y female (b). Both include an XX-bivalent (arrow) without indication of the presence of a Y in (b).

On the other hand, the XY females are anatomically normal and undistinguishable from the XX females. Both show almost identical litter sizes of about 3.4. Thus, females may not only differ in regard to the sex of their progeny, but also in the sex chromosome complement of the somatic tissues.

The observation of two female chromosome types XX and XY raises several questions :

a) Which constitution of the sex chromosomes is present in the germ cells if a female has XY in the somatic tissues ?

b) How can the presence of a Y-chromosome in the somatic tissues of a female be reconciled with the well established male-determining function of the Y-chromosome in mammalian species, or with the recent evidence that a particular Y-linked gene, controlling the presence of H-Y antigen, is critical for the differentiation of a male gonad (Wachtel *et al.*, 1975) ?

c) What is the correspondance between the two types of females differing as to offspring and the two female chromosome types ?

Attempts to answer the first of these questions show that an XX-bivalent, indistinguishable from that present in XX females (fig. 4a), occurs almost regularly in diakinesis and first meiotic metaphase of XY females (fig. 4b). Only one exception, namely the presence of an additional Y besides the XX-bivalent, has been noted as a result of studying 62 oocytes from 20 animals. Therefore, one has to assume a mechanism in XY females eliminating the Y from the germ line and replacing it by a second X which, in an XY female, ought to be an identical copy of the maternal X. Such a segregating mechanism, thought to take place in an early oogonial mitotic division and in an early developmental stage of the XY female gonad, should consist of a double non-disjunction of both daughter chromatids of the X to one pole and of those of the Y to the other (fig. 5a). Moreover, there is a possibility that a similar non-disjunction mechanism occurs in some of the XX-females (fig. 5b).

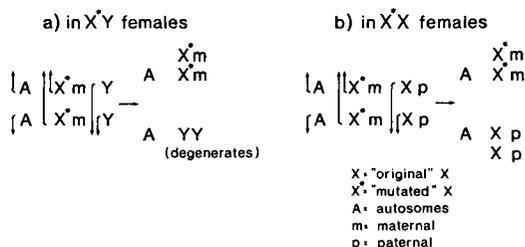


FIG. 5. — Mitotic non-disjunction in primordial germ cells or oogonia. a) in  $X^*Y$  females ; b) in  $X^*X$  females.

The second question of how the presence of a Y in an XY female is reconcilable with the male-determining function of the Y, can be answered by assuming an X-linked factor which inactivates the male-determining gene on the Y (Fredga *et al.*, 1977). This is in accordance with the lack of H-Y antigen on female XY cells in contrast to male XY cells which express this antigen on their cell surfaces (Wachtel *et al.*, 1976). The hypothesis of gene identity for H-Y and for male determination as favored by Ohno (1976),



(Frank, unpublished). Yet, while exclusively female progeny is expected in X\*Y females, some few females occur that also occasionally produce sons. In a set of data from 115 X\* Y females (Frank, unpublished), 103 had only female offspring, namely 781 daughters, and 12 exceptional females had mixed progeny with 26 daughters and 19 sons. The mean sex ratio for these 115 X\*Y females was therefore 0.02. The mean sex ratio found in the progeny of 129 XX (XX and X\*X) females was ideally almost 0.33 and it included the still low male ratio of 0.27 observed in 83 of those « XX females » that had X\* Y mothers and daughters (which means that they were X\*X-females).

So far, there is correspondance, at least along the major lines, between both reproductive females types, F and MF, and the chromosomal types. But the exceptional occurrence of X\* Y females with sons remains to be explained by further studies. Certainly such females cannot be regarded as abnormal. On the contrary, they seem to belong to a small category of their own, and sometimes repeated occurrence of sons is observed. As an explanation, it was thought in those cases that the postulated double non-disjunction mechanism might be defective, but so far only meiotic metaphases with XX-bivalents have been found in meiotic preparations of X\*Y females with sons. However, as already mentioned before, one M1 figure, indicating possible irregularities of the assumed mitotic non-disjunction mechanism, was observed in a (regular) X\* Y female. This could at least explain the not infrequent sex chromosome abnormalities in this species (Gropp *et al.*, 1976), if not the occurrence of XY sons of XY mothers.

There is certain evidence that the phenomena observed in the wood lemming may be of a more general biological interest.

a) The hypothesis can be advanced that a regulator system is involved, permitting population dynamics control via regulation of the sex ratio (Hamilton, 1967). It goes without saying that the transition from a permanent low density population to a peak would be enhanced by a switch from XX to X\*Y or from the MF to the F-type female. How such regulation could work is still unknown and constitutes a subject for further study.

There are many examples, mostly among small rodents, of drastic changes in population density. The wood lemming system opens a cytological approach to an understanding of population dynamics mediated by cytogenetic conditions.

b) The situation in the wood lemming is not so surprising if it is remembered that there are more systems in *Microtinae* showing peculiarities of chromosomally mediated sex determination, as in *Microtus oregoni* (Ohno *et al.*, 1963, 1966) or in *Ellobius lutescens* (Castro-Sierra and Wolf, 1967 ; Nagai and Ohno, 1977).

c) Finally, as far as the postulated male-female sex reversal mutation in the wood lemming is concerned, there is at least one comparable condition in man. In view of the evolutionary conservation of the mammalian X-chromosome (Ohno, 1967), it has been argued that the mutation in familial cases of XY pure gonadal dysgenesis can be homologized with the mutation in the wood lemming (Wachtel *et al.*, 1976). Whether there are other such examples will be determined by further studies.

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**Résumé.** Le wood Lemming (*Myopus schisticolor* L.) montre certains caractères particuliers. a) La sex ratio montre une prévalence des femelles et quelques femelles produisent seulement des descendants femelles. b) Une grande proportion des femelles possèdent les chromosomes XY dans les tissus somatiques, mais le Y est absent des cellules germinales des lignées étudiées. c) Nous postulons donc l'existence d'un mécanisme de double non disjonction au début de la vie embryonnaire, éliminant le chromosome Y des cellules germinales et le remplaçant par une replication du chromosome X. d) On pense que l'X des femelles XY porte un facteur d'inversion du sexe qui affecte l'action de déterminant mâle de l'Y. e) Il est évident que dans la plupart des cas les femelles X\*Y sont celles qui ne produisent que des filles ; mais (f) quelques exceptions suggèrent que la régulation selon (c) et peut-être selon (d) est incomplète. De plus les aberrations de chromosomes sexuels existent dans cette espèce. Elles peuvent être également attribuées, au moins pour une part, à un défaut dans les mécanismes suggérés pour assurer le changement de l'X\*Y des cellules somatiques en X\*X\* dans les cellules germinales. Evidemment, les conditions cytogénétiques spéciales de *Myopus schisticolor* contribuent à modifier la sex ratio qui, en soi, influence probablement ou même détermine l'évolution de la densité de la population. Il n'est pas impossible que la situation de ce lemming soit un modèle d'un principe d'évolution et d'écologie également en œuvre chez quelques autres espèces.

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