

wo es inzwischen bei Isopoden gelang, näheren Aufschluss zu gewinnen: Bei *Armadillidium vulgare*^{10,15} und *A. nasatum*^{10,16} sowie bei *Tecticeps*¹⁷ wurde Heterogamete der ♂♂ gefunden, bei *Idotea balthica*¹⁸ und *Porcellio dilatatus*¹⁹ dagegen Heterogamete der ♀♀, dasselbe zwar auch bei *Jaera marina*²⁰, als weitere Besonderheit hier jedoch mit multiplem X. Ausserdem spricht für die Annahme, dass Gonosomenmechanismen bei Isopoden Neuentwicklungen darstellen, der Umstand, dass in mehreren der ohnehin seltenen Fälle in die Determination

des Geschlechts durch die Gonosomen andere Faktoren noch eingreifen: autosomale Geschlechtsrealisatoren bei *Idotea*¹⁸ sowie bei *A. nasatum*¹⁶, Umwelteinflüsse, und zwar die Tageslänge, bei *A. vulgare*²¹. Und in die gleiche Richtung weist schliesslich die Beschränkung der Gonosomenmechanismen auf bestimmte Populationen einer Art. Hierin steht *C. convexus* nicht allein: Bei *A. vulgare* wurden ganz extreme Unterschiede zwischen Populationen in bezug auf die GB festgestellt¹⁰, die sich schon in den Würfen der ♀♀ aus dem Freiland zeigen (Figur 2). Auch die Befunde bei *Haplophthalmus danicus*⁹ sind vielleicht vergleichbar.

Summary. In two strains of *C. convexus*, an Isopod which is known to be sex-determined by a polygenic system, monofactorial sex determination has been found. This is considered to be the result of an evolutionary step from polygenic to gonosomal sex determination within the species.

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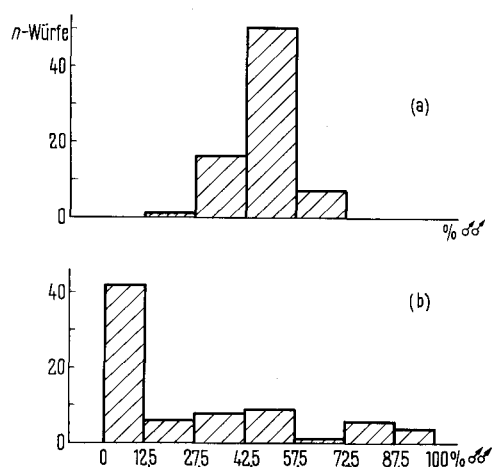


Fig. 2. ♂-Prozente in Würfen der ♀♀ aus dem Freiland von *Armadillidium vulgare*. (a) Aus den Populationen Lüneburg und Lauenburg; (b) aus der Population Lägerdorf.

¹⁵ W. LUEKEN, unveröffentlicht.

¹⁶ W. LUEKEN, Z. VererbLehre 97, 345 (1966).

¹⁷ H. NIYAMA, Int. J. Cytol. 21, 38 (1956).

¹⁸ E. TINTURIER-HAMELIN, Cah. Biol. mar. 4, 473 (1963).

¹⁹ J.-J. LEGRAND, C. r. Soc. Biol. 158, 340 (1964).

²⁰ H. STAIGER und CH. BOCQUET, Experientia 10, 64 (1954).

²¹ C. BECKER-CARUS, Verh. dt. zool. Ges. Jena (1965), im Druck.

Block to Pseudopregnancy in Mice Caused by Exposure to Male Urine

An olfactory block to pregnancy in newly-mated mice, caused by the proximity of males, especially males belonging to a different (alien) strain from the stud male, has been described by BRUCE^{1,2}. Neither pregnancy nor pseudopregnancy (the expected result of an infertile mating) ensues as a result of exposure to males, and the female returns to oestrus as though mating has not occurred. Recent work suggests that the pheromones responsible for causing the pregnancy block are excreted in the urine of males^{3,4} and are associated with androgens directly or indirectly through some androgen dependent gland⁵. However, no experiments directly concerned with the effect of males on pseudopregnant females have been reported previously, and the present report deals with the effect of alien male urine on females made pseudopregnant by mating with vasectomized males.

All females and the vasectomized males were albinos of the Parkes strain. Females were separated from the stud male when the vaginal plug was found (day 0) and housed singly. 24 h later (day 1 of pseudopregnancy) the females received one of the following treatments: (1) exposure to fresh urine from 12 CBA males on days 1–3 post coitum, in the arrangement described elsewhere⁴; (2) exposure to the same situation as in the previous case, except that

urine from CBA males was prevented from reaching the females (urine controls); or (3) left undisturbed after separation from the vasectomized males. Daily vaginal smears were examined from all females up to day 7 post coitum, and, as in the case of pregnancy block^{2,4}, a return of vaginal cornification within this period was taken to indicate a pseudopregnancy failure. The results are summarized in the Table.

Effect of alien male urine on pseudopregnant females

Treatment	Proportion and % of females with pseudopregnancy block	Proportion and % of females remaining pseudopregnant
Urine of CBA males	48/54 (89%)	6/54 (11%)
Urine controls	10/54 (19%)	44/54 (81%)
Undisturbed	2/10 (20%)	8/10 (80%)

¹ H. M. BRUCE, Nature 184, 105 (1959).

² H. M. BRUCE, J. Reprod. Fert. 7, 96 (1960).

³ C. J. DOMINIC, J. Reprod. Fert. 8, 266 (1964).

⁴ C. J. DOMINIC, J. Reprod. Fert. 11, in press (1966).

⁵ C. J. DOMINIC, J. Reprod. Fert. 10, 469 (1965).

It is evident that exposure to alien male urine causes the failure of pseudopregnancy in 89% of females, which is very close to the % of pregnancy failure obtained in newly-mated females by exposure to the proximity^{1,2} or the urine^{3,4} of alien males. In the female mouse, even if mating does not lead to pregnancy, it induces pseudopregnancy, so that oestrus is held in abeyance for about 2 weeks. The failure of mating to break the 5-day rhythm is rare. Hence it is obvious that the pheromones from males cause the failure of luteotrophic activity and stimulate the gonadotrophic activity of the adenohypophysis, resulting in oestrus and ovulation⁶⁻⁸. Incidentally this also provides a further example of the accelerating influence of the male on oestrus which has been described for several species of mammals, including the unmated female mouse⁹.

Zusammenfassung. Mäuseweibchen, die durch Paarung mit vasektomierten Männchen scheinträchtig gemacht worden waren, wurden dem Urin von Männchen eines anderen Stammes ausgesetzt. Dadurch wurde die Pseudo-

gravidität unterbrochen. Diese Beobachtung gleicht der Unterbrechung der Trächtigkeit frisch begatteter Weibchen durch den Urin fremdstämmiger Männchen und bestätigt auch die Beschleunigung des Eintritts des Östrus durch die Gegenwart der Männchen.

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Physiological Laboratory, University of Cambridge (England), April 11, 1966.

⁶ A. S. PARKES, Proc. IVth Int. Congr. Anim. Reprod., The Hague, 1961, p. 163.

⁷ A. S. PARKES and H. M. BRUCE, Science 134, 1049 (1961).

⁸ C. J. DOMINIC, J. Reprod. Fert. 11, in press (1966).

⁹ My thanks are due to Professor A. S. PARKES and to Miss H. M. BRUCE for advice, and to the Population Council and the Ford Foundation for financial assistance.

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Mutual Replaceability of Amide and Ester Groups in Biologically Active Peptides and Depsipeptides

As is well known, the ester group not only models the amide group in its spatial characteristics, but is quite similar to it in electron density distribution. One could therefore expect that analogues of naturally occurring biologically active peptides and depsipeptides, wherein the ester group is replaced by the amide group and vice versa, would be very similar to the original compounds in both steric structure, i.e. topologically, and the electronic nature of the functional centres. Such topochemically similar compounds should therefore possess quite similar electronic and steric complementarity to the same receptor and, as a result, the analogues should also manifest high biological activity. These premises were the starting point of our studies on the structure activity relations of peptide and depsipeptide compounds.

The first object of these studies was the depsipeptide antibiotic valinomycin (I, Table I). Analogues of this antibiotic (II–IV) in which one of the hydroxy acid residues was replaced by an amino acid of the same type and configuration were found to possess a biological activity, in a number of cases equal to or exceeding the activity of the natural compound.

On the other hand, we replaced the amide groups by ester groups in the biologically active peptides glutathione, ophthalmic acid and bradykinin¹⁻⁵. The resultant depsipeptide analogues, namely Glyc³-glutathione, Glyc³-ophthalmic acid, Glyc⁴-bradykinin, Glyc⁶-bradykinin and Glyc^{4,6}-bradykinin, partly or wholly retain the activity of their natural counterparts. In particular, with respect to the glyoxalase system (glyoxalase I) Glyc³-glutathione exhibits 75% of the activity of glutathione, while, with respect to the formaldehyde/NAD-oxidoreduction system, its activity equals that of glutathione. At the same time ophthalmic acid in the glyoxalase system depresses

the activity of glutathione by 60% and Glyc³-ophthalmic acid by 35%. Moreover, ophthalmic acid does not depress the activity of glutathione in the formaldehyde/NAD-oxidoreduction system, whereas its depsipeptide analogue does so to the extent of 30%. Data on the biological activity of the depsipeptide analogues of bradykinin are summarized in Table III.

Table I

No.	Compound*
(I)	$\left[\text{D-Val-L-Lac-L-Val-D-HyIv} \right]_3$ (Valinomycin)
(II)	$\left[\text{D-Val-L-Ala-L-Val-D-HyIv}-(\text{D-Val-L-Lac-L-Val-D-HyIv})_2 \right]$
(III)	$\left[\text{D-Val-L-Lac-L-Val-D-Val}-(\text{D-Val-L-Lac-L-Val-D-HyIv})_2 \right]$
(IV)	$\left[\text{D-Val-L-Val-L-Val-D-HyIv}-(\text{D-Val-L-Lac-L-Val-D-HyIv})_2 \right]$

* The synthesis of compounds (II–IV) will be described in another paper.

¹ L. A. SHCHUKINA and A. L. ZHUZE, Proceedings of the Fifth Peptide Symposium, Oxford 1962 (Pergamon Press, Oxford 1963), p. 189.

² L. A. SHCHUKINA, A. L. ZHUZE, E. P. SEMKIN, and S. N. KRASNOVA, Izv. Akad. Nauk SSSR, Ser. Khim. 1964, 685.

³ L. A. SHCHUKINA, G. A. RAVDEL, M. P. FILATOVA, and A. L. ZHUZE, Acta chim. hung. 44, 205 (1965).

⁴ L. A. SHCHUKINA, G. A. RAVDEL, and M. P. FILATOVA, Khimiya Prirodnikh Soedinenii, in press.

⁵ L. A. SHCHUKINA and A. L. ZHUZE, Zh. obshch. Khim., in press.