dently acting genes are important; however, with time $\sigma^2_{s.c.a.} = \sigma^2_D$ increases, so that *specific* crosses and hence specific gene combinations become progressively more important.

The other temporal variation observed was the progressive reduction in the discrepancy between the inbreds and hybrids with time, i.e. the inbreds, although taking longer to mate, eventually tend to catch up with the hybrids.

In conclusion, therefore, the genotype exerts an extremely important influence on the time flies take to mate. Since this must be an important component of fitness, any variations in times occurring in the wild must be of evolutionary significance.

Résumé. Chez quelques lignées pures et hybrides de *Drosophila melanogaster* l'accouplement sexuel s'effectue avec des vitesses variables. On peut conclure que la constitution génotypique exerce une action très importante sur la vitesse de l'accouplement.

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A Biologically Active Analogue of Oxytocin not Containing a Disulfide Group

A conspicuous structural feature in the molecule of oxytocin (I, $X = S$, $R = NH_2$) and related neurohypophysial peptides is the presence of a twenty-membered ring incorporating the disulfide bond of a cystine residue[1,2]. It early appeared that this structural feature was necessary for biological activity since desulfuration of oxytocin[3,4] or its reduction followed by alkylation[5,6] gave biologically inactive products[7]. Recent work[8] has confirmed early claims[9,10] that the reduced form of oxytocin, now known to be the acyclic cysteine peptide, has no uterotonic activity. The results of studies on a range of synthetic oxytocin analogues, as recently summarized and discussed by JARVIS and DU VIGNEAUD[11], have shown that any change in the size of the ring incorporating the disulfide group led to a sharp decrease, or complete disappearance, of biological activity. Such an effect might be ascribed either generally to a change in the topochemistry of the molecule, resulting from the change in ring size, or more specifically to its influence on the reactivity of the disulfide bond. SCHWARTZ, RASMUSSEN et al.[12], in a series of studies, established a correlation between the biological effects of oxytocin and vasopressin on the kidney and toad bladder, and the amount of radioactivity bound to the target tissue after administration of the labelled hormone and released from it by treatment with thiols. It was plausibly suggested[12] that at any rate one of the molecular events leading to the manifestation of biological activity involved reaction of the disulfide group of the hormone with sulfhydryl groups on the receptor with formation of a hormone-receptor disulfide bond.

In order to establish unequivocally whether the role of the disulfide bond in the biologically active molecules is essentially chemical, i.e. connected with its special reactivity, or purely structural, an analogue would be required which would closely resemble one of the active hormones in its steric and hence topochemical properties but would lack the reactive disulfide bond. A structure with one of the sulfur atoms of the disulfide group replaced by a methylene would meet this requirement since the change from S-S to CH_2-S can be regarded as approximately isosteric. We have now completed the synthesis of such a 'carba' analogue in the oxytocin series. For greater preparative convenience we chose in the first instance to synthesize a derivative lacking the terminal amino group (I, $X = CH_2$, $R = H$); this appeared justified as DU VIGNEAUD et al.[13–15] had demonstrated that this amino group is not essential for biological activity.

The protected octapeptide amide III, obtained as the hemihydrate, m.p. 214–217°, from the heptapeptide amide[14,16] II and benzyloxycarbonyltyrosine azide[17], was reduced with sodium in liquid ammonia and alkylated *in situ* with tert-butyl 4-iodobutyrate. The crude reaction product was treated with acid to split the tert-butyl ester grouping and the S-(3-carboxypropyl)octapeptide amide

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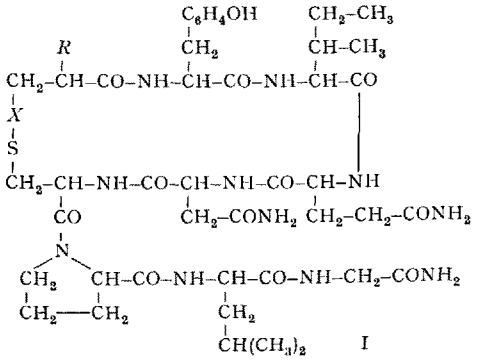
IV was isolated in an analytically pure state as the dihydrate, m.p. 145–147°, by elution from a column of Dowex 1 with a decreasing pH gradient (pyridine-acetic acid) at about pH 5.5. The peptide was cyclized by treatment with N-ethyl-5-phenylisoxazolium-3′-sulfonate[18] in dimethylformamide under high-dilution conditions[19]. The cyclic product (I, $X = CH_2$, $R = H$), which may be named as the lactam of tyrosyl-isoleucyl-glutaminyl-asparaginyl-S-(3-carboxypropyl)cysteinyl-prolyl-leucyl-glycine amide, was isolated after deionization on ion exchange columns as an electrophoretically and chromatographically homogeneous, neutral, ninhydrin-negative material giving a positive Pauly reaction and iodoplatinate(IV) reaction for sulfur. Analysis of the lyophilized product for nitrogen indicated a peptide content of 80%. Amino acid analysis[20] showed the presence of all the expected amino acids (including S-(3-carboxypropyl)cysteine) in equimolecular amounts, except for tyrosine, for which low values were found; we believe this to be due to decomposition rather than inhomogeneity of the product.



Ile·Glu(NH_2)·Asp(NH_2)·Cys(Bzl)·Pro·Leu·Gly·NH_2 II

↓ Z·Tyr·N_3

Z·Tyr·Ile·Glu(NH_2)·Asp(NH_2)·Cys(Bzl)·Pro·Leu·Gly·NH_2 III

↓ 1) Na/NH_3; $I(CH_2)_3CO_2Bu^t$ 2) CF_3COOH

Tyr·Ile·Glu(NH_2)·Asp(NH_2)·Cys·Pro·Leu·Gly·NH_2 IV

HO·CO·CH_2·CH_2·CH_2

↓

I, $X = CH_2$, $R = H$

When assayed on the rat uterus *in vitro* under standard conditions[21], the analogue had an activity corresponding to about 60 IU/mg; the avian depressor activity[22] was about 25 IU/mg, and the antidiuretic activity in the hydrated alcohol-anaesthetized rat[23] about 1 IU/mg. These results[24] show that at any rate these biological effects do not critically require the presence of the disulfide bond, and preclude molecular mechanisms based on the reactivity of such a bond.

Zusammenfassung. Die Synthese eines Analogen des Deamino-oxytocins, in dem ein Schwefelatom der Disulfidbrücke durch eine Methylengruppe ersetzt ist (I, $X = CH_2$, $R = H$), wird beschrieben. Die Verbindung hat oxytocinähnliche biologische Wirkungen.

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On the Expansion-Contraction Rhythm of the Sea Anemone, *Actinia equina* L.[1]

The expansion-contraction rhythms (ECR) shown by many Anthozoa have generally been interpreted as daily rhythms. However, an ECR correlated with the tide was also described[2] in *Actinia equina* L., but apparently this species also has a daily ECR[3]. According to Bohn[4], both rhythms are maintained, in the laboratory, under conditions of constant light and constant water level. This fact has been doubted by other authors[5–7].

We have studied specimens of *A. equina* from the intertidal zone of the Tyrrhenian coast. We have collected only specimens which were under the same conditions of illumination and at the same level. They were kept in the laboratory at a temperature of 20°C ± 0.5° and their activity was checked every 30 min. The observations during the dark periods were done using an infrared source and detector (sniper-scope).

The animals were divided into 6 groups: (1) *Continuous immersion, nictemeral rhythm of illumination.* Sea anemones are expanded in the dark and closed in the light. (2) *Continuous immersion, nictemeral illumination and moonlight.* The behaviour of the animals is similar to that of group 1. Moonlight does not seem to have any influence.

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