

replication, indicating that despite wide variation among subjects, there is consistency from one replication to the next.

Several factors influence the variability of taste results and could contribute to the 'uncertainty' mentioned by SHALLENBERGER¹³. (a) Among several sugars, concentration has a marked effect on taste differences. SHALLENBERGER's conclusion that β -D-glucose was sweeter than the α -form may be attributable to tasting only crystals. (b) In compounds having multiple tastes it is difficult to assign intensity values to one sensation independent of the other. This was observed with mannose, as reported herein and by others⁸⁻¹⁰, and was also observed with xylose which appeared to have several tastes. (c) The purity of the compound obviously could contribute to variability of response. The multiple tastes of xylose

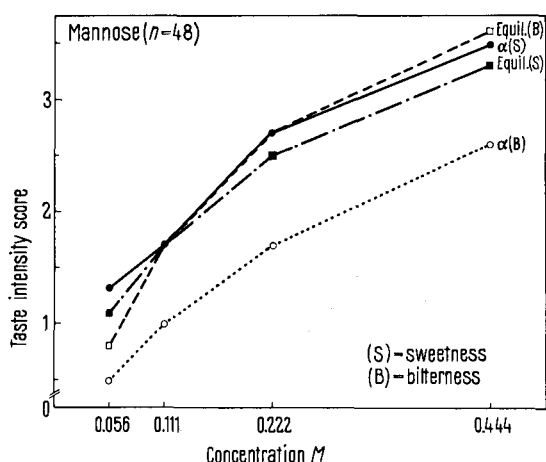
could have been due to impurities. Despite the fact that the maltose was the highest purity available, distinct differences in 'flavor' were observed between Lots No. 5319 and 2710. KARE and MEDWAY²⁰ also speculated that the inability to obtain maltose of absolute purity contributed to their results on taste discrimination by the fowl. In spite of being analytically pure, some compounds adsorb volatile, odorous constituents from the environment, e.g. from contact with paper, plastic or metal, which interfere with a true taste response. (d) It is recognized that subjects differ in sensitivity, as well as in their estimation of intensity and interpretation of quality. This can be minimized by careful selection and training.

Despite the variability mentioned above, this investigation reconfirms that there are distinct differences in taste between configurations of these anomeric carbohydrates. Both quantitative and qualitative gustatory properties can be measured reliably by trained human subjects, thus providing a basis upon which molecular biologists can elucidate the causative mechanisms.

Zusammenfassung. Es wurden quantitative und qualitative Geschmacksvergleiche zwischen frisch zubereiteten und ins Gleichgewicht gebrachten Lösungen von Fruchtzucker, Mannose, Malzzucker, Xylose und Rhamnose angestellt. Erfahrene Versuchspersonen stellten in bestimmten Zeitintervallen die Geschmackswirkung der Lösung fest, die mit polarimetrischen Zeitmessungen verglichen wurden.

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Intensity of sweetness and bitterness of 4 concentrations of freshly prepared and equilibrium solutions of α -D-mannose. (0 = none; 8 = extreme.) Each point represents 48 individual judgments.

²⁰ M. R. KARE and W. MEDWAY, Poultry Sci. 38, 119 (1959).

²¹ We gratefully acknowledge the participation of the subjects and the technical assistance of Mrs. IDA M. TRABUE.

About a Possible Participation of Nucleic Acids in Synaptic Transmission

Some time ago, while studying the parasympathetic regulation of cardiac rhythm in *Rana temporaria*^{1,2}, some evidence was obtained which might imply an involvement of RNA in synaptic function. This finding is now reported in detail. The choice of neuromyocardial synapses for experimentation was suggested by several data found in the literature. An effect of nucleic acids and nucleotides on the conduction system and on the refractory period of the heart was observed by DRURY and SZENT-GYORGYI³ and by DRURY⁴. In 1956 ROBB⁵ reported that, after stimulation of the vagus nerve, nucleic acid derivatives in the dog heart differed from those present when the sympathetic nerve was stimulated. The neuromyocardial system had also the advantage of being well known and readily accessible to quantitative experimentation.

The experiments were performed on *R. temporaria* hearts perfused with Ringer's solution. The cardiac rhythm was blocked by stimulating the nuclei of the vagus nerve or the

sensory area of the splanchnic by means of electrodes². Blockage was also obtained by acetylcholine ($1.0 \cdot 10^{-6} M$). Neutral tryptaflavine⁶ ($1.0 \cdot 10^{-4} M$) was dissolved in Ringer's solution.

Figure 1 shows that tryptaflavine $1.0 \cdot 10^{-4} M$ is capable of inhibiting the blocking action on the heart caused by electric stimulation of the nuclei of the vagus or of the receptive field of the splanchnic; it can also inhibit the blocking action of acetylcholine. The duration of the tryptaflavine effect is longer in the case of electrical stimulation of the splanchnic area than in the case of the

¹ P. VOLPE, Boll. Soc. ital. Biol. sper. 7, 4 (1962a).

² P. VOLPE, Boll. Soc. ital. Biol. sper. 7, 5 (1962b).

³ A. N. DRURY and A. SZENT-GYORGYI, J. Physiol. 68, 213 (1929).

⁴ A. N. DRURY, Physiol. Rev. 16, 292 (1936).

⁵ J. S. ROBB, Am. J. Physiol. 187, 626 (1956).

⁶ A mixture of 2,8-diamino-10-methylacridinium chloride and of 2,8-diaminoacridine containing, when dried at 105°C for 2 h, not less than 13.3% and not more than 15.8% of Cl. The nitrogen is about 16.2%.

blockage produced by acetylcholine or by vagus stimulation. The effect of tryptaflavine may be interrupted by addition of RNA to the Ringer's solution (Figure 2): when the blockage of the cardiac rhythm is produced by stimulation of the vagus or of the splanchnic field or by addition of acetylcholine. Analogous results can be obtained by using some RNA derivatives, such as guanylic and adenylic acids, guanine and adenine. These data indicate that the action of tryptaflavine is reversible, as expected from a loose type of binding.

The use of tryptaflavine in the attempt to verify the possible involvement of RNA or RNA derivatives in synaptic function was suggested by indications that proflavines can form insoluble complexes with nucleic acids and their derivatives *in vivo*⁷⁻⁹, and that the formation of these complexes is reversible⁹. Recent work indicates that proflavines combine both with free nucleotides and RNA (as well as with DNA) and inhibit, in particular, the synthesis of RNA and proteins¹⁰. Proflavines have also been shown to interfere with messenger RNA and to inhibit the DNA-dependent step in the synthesis of RNA; reversal of this inhibition can be obtained with DNA¹¹.

Furthermore, some authors maintain that acriflavines are mutagenic for organisms, by virtue of interaction with nucleic acids¹². This supports the hypothesis that the effect of tryptaflavine on neuromuscular synapses might be due to a binding of this compound to nucleic acids or nucleic acid derivatives. However, other interpretations are possible. Future work should establish whether or not the first of these alternatives is the only possible one¹³.

⁷ H. McILWAIN, *Biochem. J.* **35**, 1311 (1941).

⁸ J. BRACHET, *C. r. Soc. Biol. (Paris)* **140**, 893 (1946).

⁹ P. B. WEISZ, *J. cell. comp. Physiol.* **46**, 517 (1955).

¹⁰ C. SHOTTISSEK and R. ROTT, *Nature* **204**, 39 (1964).

¹¹ R. L. SOFFER and F. GROSS, *Bioch. Biophys. Acta* **84**, 423 (1964).

¹² L. S. LERMAN, *J. cell. comp. Physiol., Suppl. I*, **64**, 1 (1964).

¹³ Thanks are due to Professors J. BRACHET, University of Brussels, and A. GIUDITTA, International Laboratory of Genetics and Biophysics, Naples, Italy, for fruitful and stimulating discussion. The experimental work has been carried out at the Physiology Institute of Moscow University in 1960.

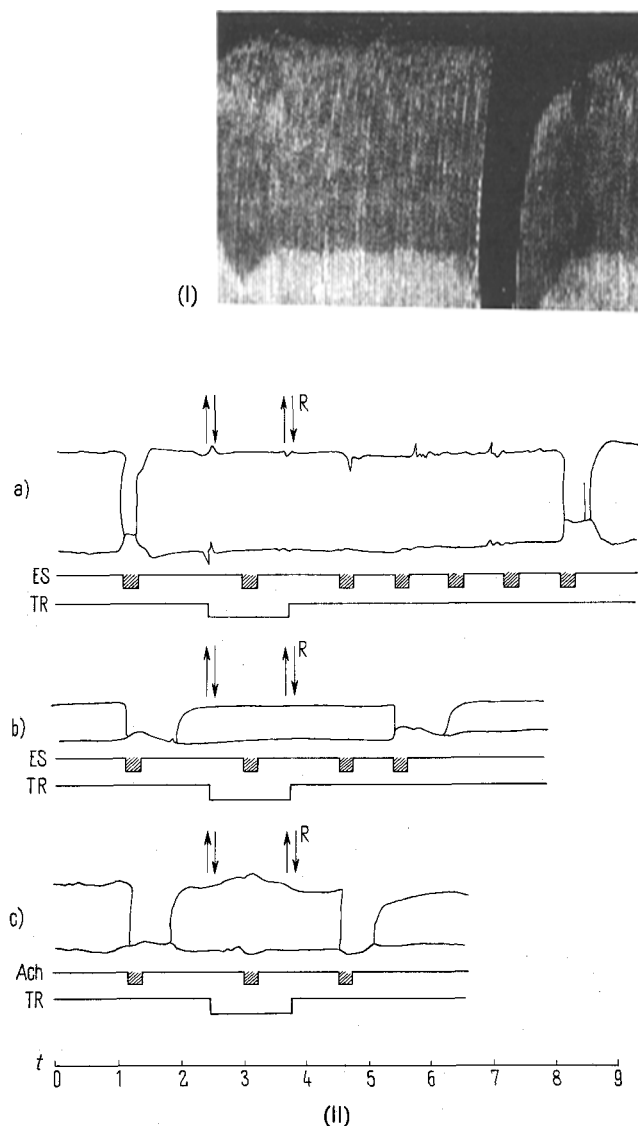
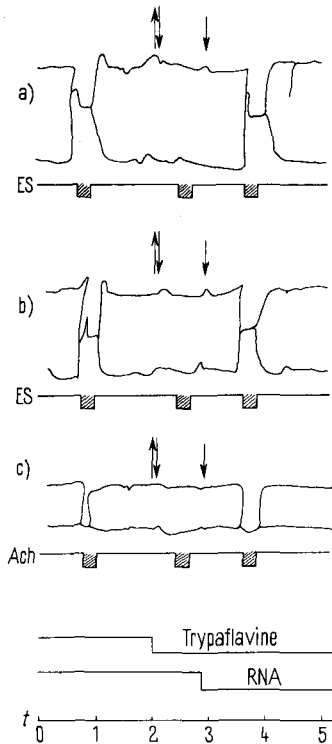


Fig. 1. Tryptaflavine effect. The kymogram above (I) shows a typical effect of the vagus on the heart: electrical stimulation of the nerve brings about immediate blockage of the cardiac rhythm (time is shown in 5 sec intervals; the distance between the solenoids is 14 cm). This kymogram serves as standard in interpreting the other kymograms, which are presented schematically. The tryptaflavine effect (II) is revealed as: (a) inhibition of the electrical stimulation of the sensory field of the splanchnic nerve; (b) inhibition of the electrical stimulation of the nuclei of the vagus; (c) inhibition of acetylcholine action. In all cases it is apparent that, after perfusion of the heart with tryptaflavine, the blocking of rhythm attributable to the vagus no longer takes place; however, it reappears after washing with Ringer's solution (ES = electrostimulation, solenoids 14 cm apart; TR = tryptaflavine $1.0 \cdot 10^{-4} M$ in Ringer's solution; Ach = acetylcholine $1.0 \cdot 10^{-6} M$; t = time in min). Note that the renewed effect of the vagus after tryptaflavine is enormously retarded in (a) as compared with (c).



Riassunto. La triptaflavina, quale complessante in vivo degli acidi nucleici e dei nucleotidi, è capace di bloccare al livello delle sinapsi neuromiocardiche l'effetto del vago. Viene presa in considerazione la possibilità che l'RNA possa essere in qualche maniera implicato nella trasmissione sinaptica, in particolare, nel meccanismo d'azione dell'acetilcolina.

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Fig. 2. Interruption of the tryptaflavine effect by RNA. The kymographs show that the effect of the tryptaflavine disappears when RNA is added to the Ringer's solution. The blocking of heart rhythm by the vagus was brought about in 3 ways: (a) electrical stimulation of the sensory area of the splanchnic nerve; (b) electrical stimulation of the nuclei of the vagus; (c) acetylcholine. In all 3 cases note that stimulation of the vagus no longer blocks the heart rhythm after perfusion with tryptaflavinated Ringer's solution (as in I); whereas the addition of RNA alone causes the blockage to reappear (ES = electrostimulation, solenoids 14 cm apart; TR = tryptaflavine $1.0 \cdot 10^{-4} M$ in Ringer's solution; RNA = 10 O.D.₂₆₀/ml added; t = time in min).

THEORIA

Beitrag zur Theorie der konvexen Bereiche der euklidischen Ebene

A. Ein ebener konvexer Bereich wird charakterisiert durch folgende Masszahlen: Breite in der Richtung φ , $b(\varphi)$; Dicke, Δ , kleinste Breite; Durchmesser, D , grösste Breite; Umfang oder Länge, L ; Flächeninhalt, F . Bei konvexen Bereichen konstanter Breite fallen Dicke und Durchmesser zusammen.

Es lassen sich nun die mannigfachen Extremalprobleme aufstellen, die auf Ungleichungen zwischen den beteiligten Masszahlen führen. Je nach der Zahl der beteiligten Masszahlen unterscheiden wir Probleme der Stufen I, II, III.

B. Die Probleme der Stufe I sind restlos gelöst. Am wenigsten bekannt dürften folgende Ungleichungen sein:

$$\frac{\sqrt{3}}{3} \Delta^2 \leq F < \infty. \quad (\text{Gleichheitszeichen nur für das gleichseitige Dreieck mit 3 Höhen } \Delta) \quad (1)$$

$$\frac{b^2}{2} (\pi - \sqrt{3}) \leq F \leq \frac{b^2}{4} \pi. \quad (\text{Gleichheitszeichen links nur für das reguläre Kreisbogendreieck, rechts nur für den Kreis}) \quad (2)$$

Gleichseitiges Dreieck und reguläres Kreisbogendreieck spielen in den folgenden Ausführungen eine ausschlaggebende Rolle.

C. In den Problemen der Stufe II sind alle Maxima von F und die Extrema von $L(\Delta, D)$ bekannt. Betreffend Minima von F existieren drei Lücken, nämlich:

$$F_1 \leq F \leq \frac{\Delta}{2} \sqrt{D^2 - \Delta^2} + \frac{D^2}{2} \arcsin \left(\frac{\Delta}{D} \right); \quad \left[\frac{\sqrt{3}}{2} D < \Delta \leq D \right] \quad (3)$$

$$F_1 \leq F \leq \frac{\Delta L}{2} - \frac{\Delta^2}{4} \pi; \quad [\pi \Delta \leq L < 2 \sqrt{3} \Delta] \quad (4)$$

$$F_1 \leq F \leq F_2; \quad [3 D < L \leq \pi D] \quad (5)$$

(F_2 wird im ganzen Intervall $2 D \leq L \leq \pi D$ durch die «symmetrische Linse»¹ realisiert.)

D. Es ist nun leicht einzusehen, dass in den Problemen (3)–(5) die unbekannte Extremalfigur einer Schar von zulässigen Bereichen angehören muss, die zwischen den in B genannten Extremalbereichen interpoliert. Es ist insbesondere das reguläre Kreisbogendreieck als letztes Glied der Kette durchwegs extremal².

E. Im Problem (3) vermute ich, dass die noch unbekannte Extremalfigur folgendermassen konstruiert werden kann: In den Eckpunkten eines gleichseitigen Dreiecks mit der Seite D errichtet man je einen Kreisbogen mit Radius Δ , wobei Δ grösser als die Höhe, aber kleiner als die Seite des Dreiecks ist. Sodann bildet man von den Eckpunkten aus mit 6 Tangentenstrecken die konvexe Hülle der drei Bogen³.

¹ Durchschnitt zweier gleich grosser Kreise mit Durchmesser D und Randlänge L .

² Die Extremaleigenschaft des regulären Kreisbogendreiecks ist bis jetzt übersehen worden.

³ Hier ist die Vermutung neu. Für das Problem (4) ist sie bereits von YAMANOUTI ausgesprochen worden.