Effect of emetine $4 \times 10^{-6} M$ on incorporation of ^{14}C-labeled precursors

^{14}C Precursor	Inhibition of incorporation at EHT + 80 min (%)
Amino Acids	75.2±2.1 ($n = 5$)
Acetate	46.8±0.2 ($n = 4$)
Thymidine	53.8±2.1 ($n = 6$)
Uridine	4.7±3.1 ($n = 3$)

Percentages represent the mean and standard error.

organelles depend on microsomal and their own protein synthesis for assembly of their functional units[15] and both are inhibited by emetine[16]. This agent has also been noted to selectively damage mitochondria in dog heart[17].

The possibility that emetine is acting by blocking the uptake of precursors seems unlikely in light of the normal incorporation of uridine and the normal incorporation of thymidine and acetate in the early part of the experiment. RASMUSSEN and ZEUTHEN[18] have demonstrated in *Tetrahymena* that cell division is blocked by inhibition of protein synthesis and this seems the major reason why emetine is inhibiting division.

Comparing this system to GROLLMAN'S[3] work in Hela cells demonstrates a parallel effect in protein and nucleic acid synthesis. He noted that HeLa cells concentrated the drug and that higher concentrations of emetine were required to inhibit protein synthesis in cell-free preparations. This does not seem to be the case in *Tetrahymena* as $10^{-6} M$, a concentration which does not inhibit the in vivo system (results not shown) inhibits protein synthesis in cell-free preparations of *Tetrahymena*[19].

Zusammenfassung. Emetin hemmt die synchronisierte Teilung von *Tetrahymena pyriformis*, verhindert die rasche Aufnahme von Aminosäuren und verursacht offenbar eine Zellteilungshemmung.

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Ionically Induced Volume Changes of the Smooth Muscle of the Guinea-Pig *Taenia coli*

If the osmolarity of Krebs solution is doubled by addition of potassium salts of permeant anions (KCl, KNO_3), pieces of guinea-pig taenia coli muscle exposed to these solutions shrink, but fail to recover weight, in contradiction to the predictions of the Gibbs Donnan equilibrium. If the NaCl in the Krebs solution is replaced by equivalent amounts of permeant potassium salts (isosmotic potassium solution) the tissues gain little if any weight, again not obeying the predictions of the Gibbs Donnan equilibrium. Similar results have been reported by several authors[1–3].

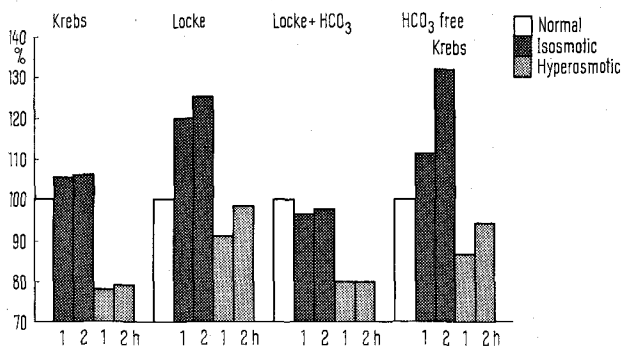

Fig. 1. The importance of HCO_3. Weight changes after exposure for 1 and 2 h to high potassium solutions. The isomotic solutions were made by replacing the NaCl in the normal solution with KNO_3, and the hyperosmotic solutions by adding 154 mM KNO_3 to the normal solutions. The results are expressed as a percentage of the weight of control pieces exposed to the normal solution. The columns are each the mean results of between 6 and 25 tissues, with standard errors of between ± 0.5 and ± 2.0.

The lack of recovery from shrinkage in hypertonic KCl or KNO_3 solution, and the lack of swelling in isosmotic K solution may suggest that the smooth muscle membrane has very low permeability to K, Cl and NO_3 ions. However, estimates of the membrane permeability to K and Cl ions from flux experiments in Krebs solution[4,5] indicate that, even assuming that high concentrations of K^+ do not increase membrane permeability, the failure of penetration of net amounts of KCl is not due to the low permeability of the membrane. Rough calculations, even using the least advantageous figures, show that sufficient ions should be able to penetrate into the cells for them to double their volume within an hour.

In order to obtain more information on the factors controlling the volume changes of the taenia, the effects of changes in the external medium were investigated. In the present set of experiments, KNO_3 has been used as the permeant potassium salt, since it has been shown[3] that NO_3 is more permeant than Cl in this tissue. Tissue pieces

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Normal solutions

(mMoles)	NaCl	KCl	$CaCl_2$	$MgCl_2$	$NaHCO_3$	NaH_2PO_4	Glucose	CO_2/O_2
Krebs solution	135.9	5.9	2.5	1.2	15.5	1.2	11.5	3/97
HCO_3^- free Krebs solution	120.4	5.9	2.5	1.2	—	1.2	11.5	0/100
Locke solution	154	5.6	2.2	—	1.8	—	5.6	0/100
Locke solution + HCO_3^-	140	5.6	2.2	—	15.4	—	5.6	3/97

Removals or additions of other salts were compensated by opposite changes in NaCl.

were dissected and mounted on stainless steel holders, and equilibrated for at least 1 h in solutions with normal K^+ concentration, before being transferred to the experimental solutions with high K^+ concentrations. After exposure, the tissues were bottled and weighed. Tissues exposed to the normal K^+ solution for similar times were also weighed in each experiment to act as controls.

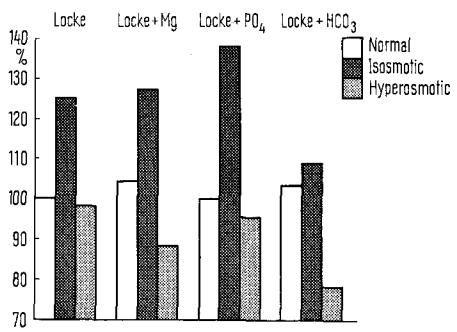

Fig. 2. Tissue weight changes after exposure for 2 h to isosmotic and hyperosmotic KNO_3 solutions; the effect of modifications of Locke solution. The weight are given as a percentage of the tissue weight in normal Locke solutions. The clear bars show tissue weights after exposure for more than 2 h to the control modified Locke solutions.

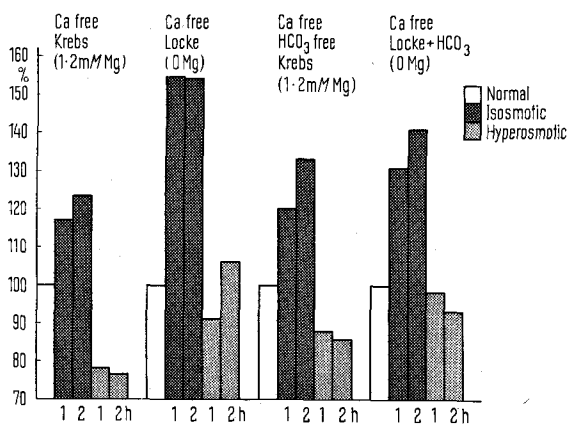

Fig. 3. The importance of calcium and magnesium. Experimental procedure as in Figure 1. The columns are each the mean results of between 6 and 17 tissues, with standard errors of between ± 0.8 and ± 3.5.

If the control solution was Locke and not Krebs solution, the behaviour of the tissues was remarkably altered, as previously noted[6] and they now behaved in a manner that would be predicted by the Gibbs Donnan equilibrium, recovering weight after an initial shrinkage in the hyperosmotic high K^+ solutions, and swelling in the isosmotic high K^+ solutions (see Figure 1).

Locke solution contains no Mg^{++}, no PO_4^{--} and only 1.8 m*M* HCO_3^- as opposed to 15.5 m*M* in Krebs solution, and it is equilibrated with 100% O_2 instead of 97% O_2 and 3% CO_2 (see Table). Figure 2 shows that of the ionic differences, the HCO_3^- is the ion that has the most significant effect. If HCO_3^- is added up to the concentration in Krebs solution, the tissues no longer swell appreciably in the isosmotic KNO_3 solution, and show little weight recovery after shrinkage in the hyperosmotic solutions. This reversal of behaviour by increasing the HCO_3^- occurs whether or not the gas mixture is 100% O_2 (pH 8.3) or 97% O_2 and 3% CO_2 (pH 7.6), although the rate of weight change may be somewhat faster at the higher pH. The importance of HCO_3^- is also shown by removal of HCO_3^- from Krebs solution. This leads to the tissues obeying the predictions of the equilibrium, and swelling in isosmotic KNO_3 solutions, and recovering weight in the hyperosmotic solutions (see Figure 1).

Divalent cations are also important in the control of tissue volume on exposure to permeant K^+ salts (see Figure 3). With no divalent cations present, the tissue swells rapidly in the isosmotic KNO_3 solution, and recovers weight after initial shrinkage in the hyperosmotic solution. This occurs whether or not HCO_3^- ions are present although HCO_3^- has some effect on the rate of weight change. In HCO_3^- containing solutions, calcium is necessary to prevent swelling when KNO_3 replaces the NaCl, and the presence of 1.2 m*M* Mg without Ca does not prevent swelling; whereas when KNO_3 is added to double the osmolarity, recovery of weight after the initial shrinkage is suppressed by either Mg or Ca.

Membrane permeability does not seem to be the limiting factor in allowing net penetration of KCl or KNO_3, as discussed above, and this is also confirmed by experiments (unpublished) which show that the fluxes of Cl^- and K^+ take place more slowly in the absence of HCO_3^- (when net penetration occurs) than they do in its presence, and this also is true in the high K^+ solutions.

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Possible explanations of these results on the volume changes may involve activation of ion pumping mechanisms, which prevent net accumulation of salts under the correct environmental conditions, or some physical restraint to volume change as could for example be imposed by protein cross linkage[7] which might depend on intracellular pH (conceivably altered by external HCO_3^-) and the presence of divalent cations.

Zusammenfassung. Analyse des unterschiedlichen Verhaltens eines glatten Muskels in Locke- und Krebs-Lösung.

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Neural Correlates of Taste Sensation Quality

It is now urgently required to clarify how human sensory experiences can be interpreted in terms of neurophysiology, or how chains of nervous events, that is, integration of spatial and temporal neural activities, in man, the whole of which is nothing but sensory experience, can be correlated with our sensation.

Concerning neural correlates of sensation quality, there are, as is well known, two major theories, the pattern theory[1] and the specificity theory[2]. Now, in agreement with the view of Hensel[3], the author believes that a certain definite pattern of nerve impulses in peripheral level, composed temporally and spatially, may convey, as a whole, a certain definite sensation quality; in other words, he believes that sensation quality might be deciphered, at least to some extent, by means of some tempo-spatial analysis of the primary afferent code.

In the case of taste sensation it is well known that there is a broad sensitivity of every receptor cell[4], multiple sensitivity of individual afferent fibres[5] (due to multiple branching of each fibre) and probably multiple innervation of each receptor cell. Taking these interrelationships between receptor cells and afferent nerve fibres into consideration, the author, using a nerve impulse count summator[6], recorded with Nitta[7] from the glossopharyngeal nerve trunk of the toad, the temporal sequence of the total sum of nerve impulses elicited during each 100 msec after the stimulation as evoked in response to various chemical stimulations of the whole tongue (Figure 1).

According to our previous investigation[8], each reaction time of 4 tastes in man at the threshold sensation was approximately 2 sec or so. Therefore, assuming that the taste quality is encoded within this short time[9], summated response curves of 4 primary taste qualities within 3 sec after the stimulation were analyzed in respect to the rate of rise, the peak time and the rate of fall in order to know which of them characterizes each curve, i.e., each quality.

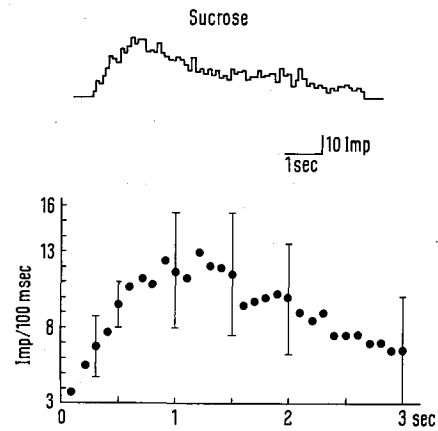

Fig. 1. Temporal sequence of summated response (above) and that of averaged values of 30 measurements (below), both to sucrose stimulation. Vertical bars mean fiducial limit ($p < 0.05$).

		RI (in 0.5 sec)	PT (sec)	RD (in 1 sec)
so	HCl, acet. ac.	14	1	3
b	QHCl, picr. ac., nicot., m-tolylurea, $MgSO_4$, sym-dimethylurea	5	1.5	3
sw	sucrose, glycine, α-dimethylurea	5	1	2
sa	NaCl, KCl, LiCl	6	0.5	2

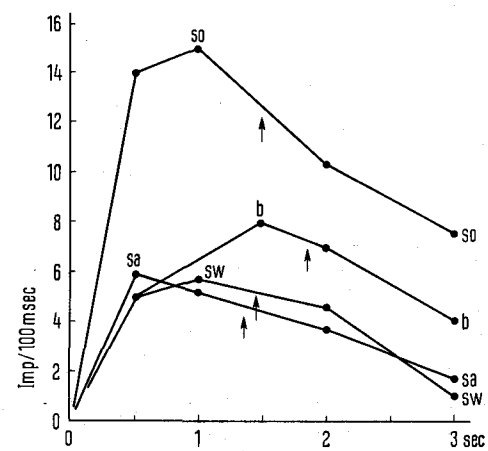

Fig. 2. Summated responses of four primary taste qualities shown as a function time. so, b, sw and sa: sour, bitter, sweet and salty quality, respectively. RI, rate of increase, means increase of impulse numbers in 0.5 sec; while RD, rate of decrease, means decrease of them in 1 sec. Arrows indicate reaction time values obtained by us previously in man[8]. Each point denotes averaged values of 30 experiments on each chemical substance.

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