duration of the Purkinje fiber action potentials vary noticeably with age (Walden and Kreher, personal communication).

According to Myerburg et al.[5], the fact that a gating mechanism is located in every false tendon may be a source of arrhythmias since alteration of only 1 of these gates can trigger re-entry. The probability that 1 of the gates is altered becomes obviously greater when the number of gates increases. From this point of view, the rabbit heart would be less exposed to certain types of arrhythmias than the dog or monkey hearts since the number of gates is limited to 3, namely the 3 bundle branches (1 in the right ventricle, and 2 in the left ventricle).

The fact that the localization of the gate is almost identical in dog and monkey and is somewhat different in rabbit is a new observation. This result is rather suprising in view of the very different morphological structures of the conducting systems in dogs and monkeys and their similarities in monkeys and rabbits.

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Effect of glycerol treatment on sodium and potassium in isolated muscle fibres of the frog

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Summary. The sodium concentration in single frog muscle fibres vacuolated by glycerol treatment was significantly higher than in devacuolated fibres. Intracellular potassium concentration did not show any significant change. It is concluded that the transverse tubular system forms vacuoles with a high NaCl concentration upon glycerol removal.

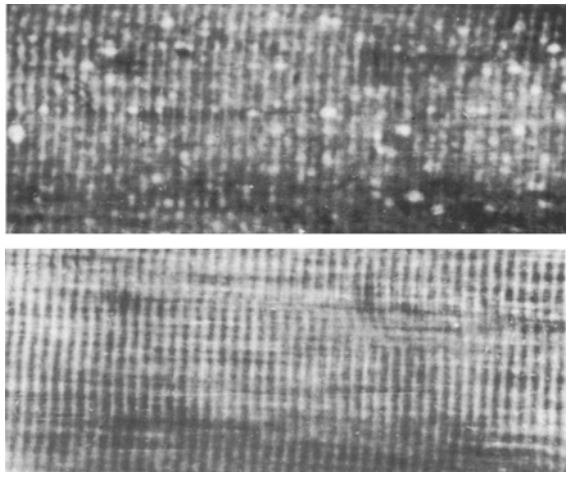
Muscle fibres, preincubated for 30 min in Ringer made hypertonic by the addition of 220 mM/l of glycerol, exhibit vacuolation of the transverse tubular system (TTS) after being exposed to normal Ringer[1,2]. Reapplication of glycerol-Ringer to vacuolated fibres results in the disappearance of vacuoles. These processes play an essential role in the decoupling and recoupling of the excitation-contraction link in muscle fibres. Recently it was shown that a TTS vacuolated by hypertonicity[3] and fatigue[4] has a high NaCl concentration. The ion content in vacuoles caused by glycerol removal is not yet clear. The purpose of this study was to compare the sodium and potassium concentrations in fibres vacuolated by glycerol removal with those in fibres devacuolated by reapplication of glycerol.

Experiments were performed on single muscle fibres isolated from the m.iliofibularis of the frog *(Rana temporaria)*. The following solutions were used: a) glycerol-Ringer (solution 1): concentration in mmole/l: NaCl 111.0, KCl 2.4, $NaHCO_3$ 2.4, $CaCl_2$ 1.8, glycerol 220.0; b) Ringer (solution 2): the same composition as for solution 1 plus a constant amount of 3.2 mmoles/l $CaCl_2$ and $MgCl_2$ without glycerol. All fibres were equilibrated for 30 min in solution 1 and after that for 30 min in solution 2. Light microscopy of these fibres revealed the presence of vacuoles distributed

The effects of glycerol removal and reapplication on sodium and potassium in skeletal muscle fibre of the frog

Group	Treatment	$[NA^+]$ mmole/kg fibre water	$[K^+]$ mmole/kg fibre water
1	Solution 1 for 30 min followed by solution 2 for 30 min	45.8±7.3 n=9	125.1±8.6 n=9
		p<0.002	p>0.1
2	The same as for group 1 followed by solution 1 for 30 min	21.8±2.0 n=15	124.8±6.8 n=14
		p>0.1	
3	Solution 2 for 120 min	25.6±2.6 n=13	
		p>0.1	
4	Solution 1 for 120 min	23.1±1.4 n=9	

Data are means±SEM. n, number of determinations; p, values were determined using Student's t-test (dispersion of $[Na^+]$ in group 1 as compared to groups 2, 3 and 4 was different). There were significant differences between $[Na^+]$ in group 3 ($p < 0.05$) and 4 ($p < 0.02$) when compared to group 1.



The light microscopic structure of frog muscle fibre ×400. *a* The vacuolated structure after washing out the glycerol. *b* The normal fibre after reapplication of glycerol.

in the entire volume of the fibres (figure a). A sample of these fibres was taken for the ion analyses (group 1). The 2nd sample of vacuolated fibres (group 2) was incubated for 30 min again in solution 1 (the procedure is termed "reapplication of glycerol"). 30 min after the start of glycerol reapplication the vacuoles disappeared and the structure of the fibres appeared normal (figure b). The devacuolated fibres (group 2) thus formed the control group. The sodium and potassium concentrations in the fibres were measured with a Perkin Elmer flame photometer and expressed in mmole/kg fibre water. The mean dry weight of fibres was taken as 19%. The cross section of the fibres was considered to be elliptical. Both the major and the minor fibre diameters were measured. All experiments were carried out at room temperature, about 22 °C.

The sodium concentration was significantly higher in vacuolated fibres as compared to devacuolated ones (45.8 mmoles/kg $H_2O \pm 7.3$ SEM and 21.8 mmoles/kg $H_2O \pm 2.0$ SEM, respectively). There was considerable fibre-to-fibre variation of the sodium concentration in vacuolated fibres, which correlated with the structure of the fibres. Intracellular potassium concentration did not show any significant change (see table). The ionic contents in group 2 were close to the values obtained in normal Ringer. The fibres held for comparison during all the experimental time in solution 2 exhibited 25.6 mmoles/kg $H_2O \pm 2.6$ SEM sodium (group 3). This value did not differ significantly from the sodium content of devacuolated fibres. It should be noted that the initial application of glycerol-Ringer did not cause a decrease in the sodium content of the fibres. The mean sodium concentration of the fibres equilibrated in normal Ringer (group 3) and glycerol-Ringer (group 4) was nearly the same (table). The structure of group 3 and 4 fibres was normal, i.e. in both cases no vacuoles were present. The values of sodium concentration obtained on isolated fibres were in good agreement with our data on whole iliofibularis muscles (extracellular space considered equal to inulin space determined on paired muscles). Sodium concentration of whole muscles expressed in mmole/kg fibre water in glycerol-Ringer (2-h-solution 1) was 23 ± 2.8 SEM ($n = 13$), after glycerol removal (2-h-solution 1 → 2-h-solution 2) 41 ± 4.4 SEM ($n = 16$) and after reapplication of glycerol-Ringer (2-h-solution 1 → 2-h-solution 2 → 2-h-solution 1) 24 ± 2.7 SEM ($n = 6$) whereas the control muscles in normal Ringer showed 25 ± 2.0 SEM ($n = 18$) sodium. It is possible that high Na concentrations in group 1 fibres may be due to the presence of numerous vacuoles in these fibres. It has been shown that the vacuoles formed from TTS by glycerol removal contain the extracellular marker ferritin (11 nm diameter) when ferritin is present in the bathing solution, both before and during the washing out of the glycerol[2]. After the vacuoles appeared they were found to be inaccessible to ferritin[2]. As free communication exists between the extracellular fluid and the lumen of TTS, it may be suggested that the increased NaCl in the vacuoles comes from the extracellular fluid. In order to account for the approximately 2-fold rise in sodium concentration in group 1 fibres the volume of the vacuoles produced by glycerol withdrawal must be about 20% of the total volume of the fibre (assuming that the concentration of NaCl inside the vacuoles is the same as that in extracellular fluid). This volume is rather close to that (15%) determined in isolated muscle fibres of the crayfish[5].

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Biological activity of the C-terminal octapeptide of cholecystokinin, of three of its analogues and of caerulein in the dog[1]

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Summary. Dose-response curves of the C-terminal octapeptide (CCK-8) of cholecystokinin, of 3 of its methoxinine analogues, and of caerulein for various variables of exocrine pancreatic secretion have been established in conscious dogs. The following relative potencies were calculated for the protein secretion activity of CCK-8 (100%), [Mox^3]-CCK-8 (52%), [Mox^6]-CCK-8 (27%), [Mox^3,Mox^6]-CCK-8 (19%) and caerulein (178%).

Cholecystokinin (CCK) is a tritriacontapeptide bearing a sulfate ester group on its tyrosine residue. Due to its complicated structure its synthesis has not yet been accomplished. Since it has been found that the biological activities of small fragments of the C-terminal end of CCK, like the octapeptide (CCK-8)[2,3], and structurally related peptides like caerulein[4] are qualitatively similar to those of the larger molecule, they are used for biological studies as well as for diagnostic purposes. The interest in these peptides has further been enhanced by the recent observation that

ED_{50} values and relative potencies of CCK-8, its analogues and caerulein for exocrine pancreatic secretion

Compound		ED_{50} pmoles/kg · h (relative potency)					
		Volume		Protein output		Bicarbonate output	
A	Asp-Tyr(SO_3H)-Met-Gly-Trp-Met-Asp-Phe-NH_2 (CCK-8)	77	(1.00)[a]	40	(1.00)[a]	79	(1.00)[a]
B	Asp-Tyr(SO_3H)-Mox-Gly-Trp-Met-Asp-Phe-NH_2 ([Mox^3]-CCK-8)	92^{NS}	(0.83)	79*	(0.52)	116^{NS}	(0.67)
C	Asp-Tyr(SO_3H)-Met-Gly-Trp-Mox-Asp-Phe-NH_2 ([Mox^6]-CCK-8)	128*	(0.60)	152**	(0.27)	166*	(0.47)
D	Asp-Tyr(SO_3H)-Mox-Gly-Trp-Mox-Asp-Phe-NH_2 ([Mox^3, Mox^6]-CCK-8)	194**	(0.39)	221**	(0.19)	243**	(0.32)
E	Pyr-Gln-Asp-Tyr(SO_3H)-Thr-Gly-Trp-Met-Asp-Phe-NH_2 (caerulein)	37	(2.10)	22	(1.78)	50	(1.57)

[a] Relative potency with respect to A. * $p < 0.05$; ** $p < 0.01$; NS = no significance (significance of the differences with respect to A).