elsewhere. In fact, data from Nea Nicomedia, a site on the Macedonian plain in northern Greece, suggest that domestic cattle were present there by 6200 B.C., the earliest known until now (*13*). The question arises: If the cattle from layers X to XII were domestic, could they have been introduced from Europe, or were they developed from the local wild population? The domestic cattle from Nea Nicomedia were apparently much smaller than the wild ox (*13*), whereas the Çatal Hüyük specimens were from an animal similar in size to their wild ancestor (Table 1). Therefore the small European race of domestic cattle does not seem to have been introduced into Anatolia, and the domestic cattle at Çatal Hüyük were developed indigenously.

It is interesting to compare the composition of the faunal sample from Çatal Hüyük with the animals represented in the frescoes and the plastic relief figures from the site. For example, relief figures of leopards and paintings of human figures in leopard skins are common, but not a single bone of a leopard was found in the collection. Similarly, the red deer is frequently represented in murals of hunting scenes, but the bones of the red deer are relatively uncommon, with the exception of shed antlers. There are figurines and paintings of the wild boar and the onager, and both of these animals are rare in the faunal collection. This presents a point that the student of prehistory should bear in mind: The plastic or graphic representation of an animal may have little relation to its economic importance. That the red deer, the onager, and the wild boar were hunted at Çatal Hüyük is beyond question, but fundamentally the people were cattle raisers (*14*). For this there is no known parallel in the Near East.

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References and Notes

1. For a description of the site, see J. Mellaart, *Anatol. Stud.* **12** (1962), and following years.
2. The total faunal sample from Çatal Hüyük is less than 2000 identifiable specimens. In contrast, the much smaller site of Suberde, situated approximately 80 km west of Çatal Hüyük and roughly contemporary with the latter's earliest levels, yielded a faunal sample of over 20,000 identifiable specimens.
3. Mellaart divided level VI into levels VIa and VIb. Many of the faunal samples from these layers have not been separated, so I have dealt with the sample from layer VI as a whole. When I was in Ankara in the summer of 1967, I found that not only had the samples from layer VI been mixed, but also those from layers X to XII.
4. The domestic dogs were identified by Miss B. Lawrence (Harvard University).
5. The 38 diagnostic elements of the artiodactyls included two necks of the scapulae, two distal ends of the humeri, four proximal and distal ends of the radii, two proximal ends of the femora, four proximal and distal ends of the tibiae, two astragali, two calcanei, four distal ends of the metapodials, eight first phalanges, and eight second phalanges. The 16 diagnostic elements for the equid material included two astragali, two calcanei, four distal ends of the metapodials, four first phalanges, and four second phalanges. The smaller number of equid diagnostic elements is due to the smaller number of elements in the equid manus and pes, and the almost total absence of limb bones. The lack of the latter is due to what I call the Schlepp effect (*6*): The limb bones of the larger game animals are left at the kill site and therefore are not found at the occupation site.
6. D. Perkins, Jr., and P. Daly, *Sci. Amer.* **219**, 5 (1968).
7. The method of calculating the relative frequency of each species is the same as the one I used in my analysis of the Shanidar fauna [D. Perkins, Jr., *Science* **144**, 3626 (1964)]. However, the number of diagnostic elements for a species may vary from site to site, depending on butchering techniques, reliability of identification, and the like. For example, the number of diagnostic elements of *Cervus elaphus* at Shanidar was 72, whereas at Çatal Hüyük the number was 38. The smaller number at Çatal Hüyük was due in part to the presence of *Bos primigenius*, which has elements in its skeleton that cannot be distinguished from *Cervus elaphus*.
8. For the method of calculating the average edible meat weight per individual, see T. E. White, *Amer. Antiquity* **17**, 4 (1952), et seq. Unfortunately, White's techniques of analysis are rarely used in the New World, and are either unknown or ignored in the Old World.
9. E. P. Walker, *Mammals of the World* (Johns Hopkins Press, Baltimore, 1964), vol. 2.
10. For a description of Can Hasan, see D. H. French, *Anatol. Stud.* **12** (1962), and following volumes. For a description of Suberde see D. Perkins, Jr., and P. Daly (*6*).
11. F. E. Zeuner, *A History of Domesticated Animals* (Hutchinson, London, 1963), p. 212.
12. See R. Lydekker, *The Ox and Its Kindred* (Methuen, London, 1912), pp. 39 and 66; F. E. Zeuner (*11*, p. 205).
13. E. S. Higgs, *Proc. Prehist. Soc.* **28**, 424 (1962).
14. Mellaart's description of the fauna from Çatal Hüyük [J. Mellaart, *Çatal Hüyük: A Neolithic Town in Anatolia* (Thames & Hudson, Bristol, 1967), p. 223] conveys a different impression. He says that domestic sheep and goats occur even in the lowest layers. In fact, there is no evidence for domestic sheep or goat at any level. There are a few sheep specimens from levels I to III that are apparently from an animal smaller than the Anatolian moufflon, but the sample is too small to be surely indicative of domestication. The remains of goats, either wild or domestic, are conspicuous by their extreme rarity in all levels. He further suggests that the hunting of wild boar and red deer was important, but neither of these animals formed a significant component of the faunal sample.

18 November 1968

Adsorption of Alkyl Trimethylammonium Chlorides at a Porous Glass–Potassium Chloride Solution Interface

Abstract. *The adsorption of dodecyl, tetradecyl, hexadecyl, and octadecyl trimethylammonium chlorides at an interface between porous glass and potassium chloride solution has been characterized by measurements of membrane potentials. The specific potential* ϕ *is 0.97* kT *per methylene group (where* k *is the Boltzmann constant and* T *is the absolute temperature) or 580 calories per mole at 23°C.*

A knowledge of the characteristics of the interface between dielectric and solution is necessary for an understanding of several phenomena, for example, flotation of mineral ores, clarification and filtration of waste materials, poisoning of ion-exchange materials, reverse osmosis, and biological membranes.

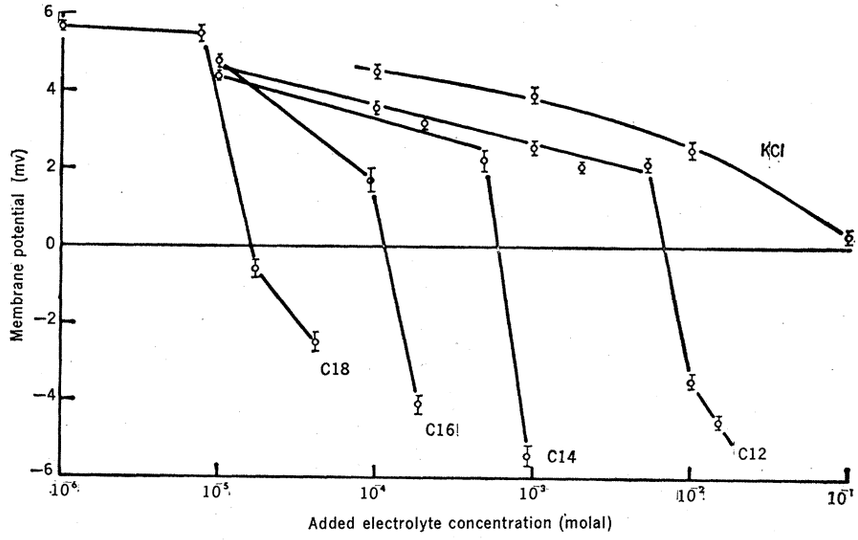

Fig. 1. Membrane potential E_M of concentration cell containing 0.05 and 0.025 molal KCl and varying concentrations of alkyl trimethylammonium chlorides plotted against concentrations of dodecyl (C12), tetradecyl (C14), hexadecyl (C16), octadecyl (C18) trimethylammonium chloride, and KCl at 23.0° ± 0.5°C and *p*H 5.8 ± 0.2.

One approach is to measure one or more of the electrokinetic effects and apply an approximate theory to calculate the distribution of electrical potential at the interface. Present theoretical interpretations of electrokinetic data in terms of double-layer structure have significant limitations (*1*). It would be useful to have alternative approaches for further evaluation of electrokinetically derived quantities.

I now report on the use of a concentration cell to study the specific adsorption of a homologous series of alkyl trimethylammonium chlorides at an interface between porous glass and KCl solution. The method has been used by De Korosy (*2*) to study qualitatively the sign reversal of ion-exchange membranes by small multivalent ions. An attempt is made here to demonstrate that a similar approach may yield a quantitative measure of the extent of charge reversal.

Porous glass membranes were immersed between two KCl solutions of molal concentrations 0.05 and 0.025, each having the same concentration of the alkyl trimethylammonium chloride. The membrane potentials E_M of concentration cells consisting of just KCl solutions and porous glass membranes have been described by the use of a modified Teorell-Meyer equation (*3*)

$$E_M = \pm \frac{RT}{F} \ln \frac{m_2 \sqrt{4m_1^2 + \overline{X}^2} + \overline{X}}{m_1 \sqrt{4m_2^2 + \overline{X}^2} + \overline{X}} \quad (1)$$

where R is the gas constant, T is the absolute temperature, F is the Faraday constant, m_i is the molality of the ith solution, and $\overline{X}$ is the effective molal concentration of fixed charge in the membrane phase. With KCl solutions the diffusion potential may be neglected because the mobilities of K^+ and Cl^- are equal in the membrane phase (*3*). The basis for the method used here is that the primary effect of the introduction of equal concentrations of alkyl trimethylammonium chlorides on both sides of the concentration cell consisting of porous glass and KCl solution is to change the sign and value of $\overline{X}$ by specific adsorption of the quaternary cation (*4*). This change in $\overline{X}$ is noted by a corresponding change in the membrane potential.

Porous glass membranes (2.2 cm by 0.025 cm) were made from a phase-separable borosilicate glass (*5*). After the membranes were leached and washed, they were heated in air at 750°C before being glued to thick-walled glass tubes. The procedure for the measurement of electromotive force (*3*) has the advantage of minimizing the junction potential at the reference electrode (*6*). The potential at each concentration of the alkyl trimethylammonium chloride is an average of at least two separate measurements made at least 15 hours apart (*7*). Measurements of potential were performed at 23.0° ± 0.5°C. The *p*H of all the solutions was 5.8 ± 0.2.

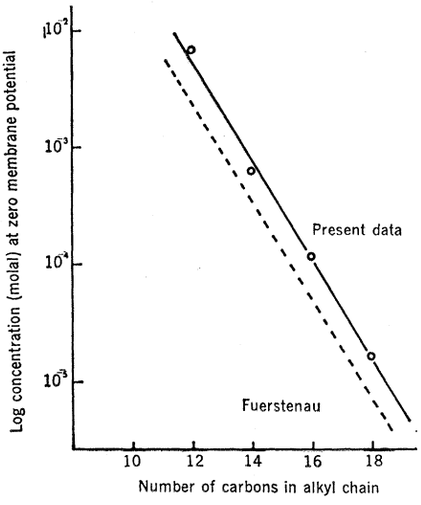

Fig. 2. Logarithm of concentration of alkyl trimethylammonium chlorides at $E_M = 0$ plotted against number of carbons in alkyl chain; dotted line from Fuerstenau and co-workers (*9*).

The potentials for the concentration cell containing 0.05 molal and 0.025 molal KCl and varying concentrations of the alkyl trimethylammonium chlorides are presented in Fig. 1. Also shown in Fig. 1 are results obtained with KCl, an indifferent electrolyte.

A decrease in E_M with the addition of an indifferent electrolyte is expected from Eq. 1. As the concentrations of the solutions in the concentration cell approach each other, E_M tends to the limit zero. This is demonstrated by the potential values obtained with solutions containing KCl. The solutions containing the alkyl trimethylammonium chlorides depart from this behavior at some critical concentration which initiates variation in potential with further addition of quaternary salt and results in a reversal in sign of E_M. This variation in potential is very similar to the streaming potentials measured by Fuerstenau for a system composed of alkyl ammonium acetate and quartz (*8*) and therefore may be explained by the use of a similar model of the double-layer interactions (*9*).

Grahame (*10*) has shown that, with certain reasonable approximations, the Stern theory for cation adsorption at an interface results in the Boltzmann equation

$$n_{oi}/n_i = L_i e^{+w_i/kT} \quad (2)$$

where n_i is the number of cations per square centimeter at the interface, n_{0i} is the number of ions of the same type per cubic centimeter of bulk solution, L_i is a correction factor which is approximately constant, k is the Boltzmann constant, and T is the absolute temperature. The work w_i required to move a surface-active cation from the bulk solution to the interfacial phase may be separated into electrostatic and chemical work, where

$$w_i = z_+ \epsilon \Psi^i + n\phi^i \quad (3)$$

Here z_+, the cation valence, is always equal to 1; ϵ is the electronic charge; Ψ^i is the electrostatic potential; and $n\phi^i$ is the nonelectrostatic or chemical work associated with the surface adsorption of an alkyl chain n carbons long. We have assumed that the chemical work is primarily confined to the alkyl segment of the alkyl trimethylammonium chloride. If we combine Eqs. 2 and 3, we have

$$\log n_{oi} = \log L_i n_i + \frac{\epsilon\Psi^i + n\phi^i}{2.303\ kT} \quad (4)$$

We assume that at $E_M = 0$, $\overline{X} = 0$ (Eq. 1). Physically, this means that the original negatively charged surface is neutralized (and then reversed in sign) by the adsorbed alkyl trimethylammonium cation. Next, we assume that $\overline{X} = 0$ implies that $\Psi^i = 0$. In this case Eq. 4 reduces to

$$\log (n_{oi})_{E_M = 0} = \log L_i n_i + n\phi^i/2.303\ kT \quad (5)$$

The quantity $\log (n_{0i})_{E_M = 0}$ is plotted against n in Fig. 2. The value of the specific potential ϕ, which may be calculated from the slope, is 0.97 kT per CH_2 group, in exact agreement with Fuerstenau's results (*9*) (the dotted line in Fig. 2). In Fuerstenau's case, the concentration of alkyl ammonium acetate at a zeta potential for quartz of zero was plotted against n. Values of ϕ determined from properties of surfactant solutions vary from 1.0 to 1.1 kT (*9*).

The shift from Fuerstenau's curve toward a higher concentration of quaternary salt is in agreement with the results Fuerstenau obtained for the zeta potential of quartz with NaCl and

dodecylammonium acetate (*8*). This he explained by postulating that, until a critical concentration of surface-active ion is reached, the concentration ratio of the two competing counterions in the surface phase is proportional to the concentration ratio in the bulk solution.

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References and Notes

1. D. A. Haydon, in *Recent Progress in Surface Science*, J. F. Danielli, K. G. A. Pankhurst, A. C. Riddiford, Eds. (Academic Press, New York, 1964), vol. 1; P. Sennett and J. P. Oliver, in *Chemistry and Physics of Interfaces* (American Chemical Society, Washington, D.C., 1965).
2. F. De Korosy, *Nature* **191**, 1363 (1961).
3. L. S. Hersh, *J. Phys. Chem.* **72**, 2195 (1968).
4. There is also the possibility of a different equilibrium distribution of the alkyl trimethylammonium chloride molecule at the two interfaces due to the different KCl concentrations. If this occurs, a membrane diffusion potential caused by the different mobilities of the quaternary and chloride ions would arise and would have an opposite sign to that of the original net Donnan potential.
5. They were given a heat treatment of 3 hours at 580°C followed by cooling at the rate of 80°C per hour. Leaching was performed in 1.0*N* HNO_3 at 95°C for 15 hours. Two washes were applied (i) 8 hours in 0.1*N* HNO_3 at at 95°C, and (ii) 60 hours in 0.05 molal KCl at 95°C. The porous glass had a pore diameter of 62 Å and a surface area of 183 m^2/g as determined by a BET (Brunauer, Emmett, and Teller) analysis with nitrogen. The fixed-charge concentration $\bar{X}$, as determined by the Meyer-Sievers method (*3*), was 0.024 molal.
6. The effect of the alkyl trimethylammonium chlorides on the reference electrodes was checked by the use of a positively charged membrane. The electrodes were checked at regular intervals for proper response without the membranes.
7. The alkyl trimethylammonium chlorides (Lachat Chemicals, Inc.) were 99.5 percent pure. Solution concentrations were checked by K. F. Sugawara, who used a spectrophotometric method coupled with a $CHCl_3$ extraction.
8. D. W. Fuerstenau, *J. Phys. Chem.* **60**, 981 (1956).
9. P. Somasundaran, T. W. Healy, D. W. Fuerstenau, *ibid.* **68**, 3562 (1964).
10. D. C. Grahame, *Chem. Rev.* **41**, 441 (1947).
11. I thank Mrs. M. C. Burke for preparing solutions and making potential measurements.

3 September 1968; revised 27 January 1969

Vitamin K and Coumarin Anticoagulants: Dependence of Anticoagulant Effect on Inhibition of Vitamin K Transport

Abstract. *Coumarin anticoagulants inhibit the release of plasma clotting factor VII by vitamin K in liver slices from vitamin K–deficient animals without inhibition of protein synthesis. When the ratio of vitamin K to coumarin anticoagulant is kept constant, but the concentrations are increased, the inhibition disappears. This suggests that the pharmacological action of coumarin anticoagulants depends on irreversible inhibition of normal vitamin K transport to its site of action. At higher concentrations of vitamin K the inhibition can be surmounted, because vitamin K can enter the cell by an alternate route that is not inhibited by coumarin anticoagulants.*

Coumarin anticoagulants act as vitamin K antagonists, since their pharmacological effect is limited to a decrease in the concentrations of the vitamin K–dependent clotting factors of plasma and can be reversed by vitamin K. Our previous work indicated that this antagonism is due to irreversible inhibition of the transport mechanism by which vitamin K normally, that is, at physiological concentrations, reaches its site of action. This inhibition can be bypassed or surmounted, because when larger doses are given vitamin K can reach its site of action by an alternate route, possibly simple diffusion, which is not susceptible to inhibition by coumarin anticoagulants. So far, this explanation has been adequate to interpret the results of many experiments that were designed to test its validity in intact animals (*1*, *2*).

The recent finding (*3*), that addition of vitamin K to liver slices from rats deficient in vitamin K as well as rats treated with a coumarin anticoagulant initiates the release of the vitamin K–dependent clotting factors of plasma into the medium, makes it possible to test the validity of the above explanation in an in vitro system. The results of such a study are reported here.

Liver slices were prepared from vitamin K–deficient rats as well as rats that had been treated with a coumarin anticoagulant (warfarin) whose plasma concentrations of factor VII were less than 5 percent of normal. One gram of slices in 10 ml of bicarbonate buffer containing uniformly labeled ^{14}C-L-leucine (2.6×10^6 disintegrations per minute) was incubated in a Dubnoff shaker at 37°C under an atmosphere of 95 percent oxygen and 5 percent carbon dioxide. After 4 hours, 0.5 ml of the medium was removed and mixed with 0.1 ml of 2 percent (by weight and volume) ethylenediaminetetraacetate (*p*H 7.4), and factor VII was determined by the method of Koller (*4*). The concentration of factor VII in the medium is expressed as the percent of factor VII, on the basis of its concentration in normal rat plasma being 100 percent. In the presence of vitamin K, the appearance of factor VII in the medium increased with time and reached a maximum between the 3rd and 4th hours of incubation.

Protein was isolated from the combined medium and slices by the method of Manchester and Young (*5*) and was assayed for the incorporation of ^{14}C-L-leucine by the liquid scintillation technique after solubilization with NCS (*6*). The efficiency of counting was between 55 and 60 percent.

Figure 1 shows the results obtained with slices from vitamin K–deficient rats. In the absence of vitamin K_1 little factor VII was found in the medium after 4 hours of incubation. Addition of vitamin K_1 at a concentration of $10^{-6}M$, the concentration required for saturation of the specific transport mechanism, increased the amount of factor VII from 1.6 to 12.0 percent. Simultaneous addition of warfarin, at concentrations of 10^{-9} to $10^{-6}M$, partially or completely inhibited this response. There were no significant differences in the incorporation of ^{14}C-L-leucine in the presence and absence of vitamin K_1 or warfarin. Thus, in slices from vitamin K–deficient animals, warfarin inhibited the response to vitamin K at concentrations that have no effect on protein synthesis.

When the experiment was carried out with slices from animals pretreated with warfarin (Fig. 2), vitamin K_1 again increased the amount of factor VII in the medium, but the concentration required to produce an equivalent response was $4 \times 10^{-4}M$ compared to $10^{-6}M$ for slices from vitamin K–deficient animals. A similar, approximately 100-fold difference has been found between the potency of vitamin K_1 in vitamin K–deficient rats compared to those treated with a coumarin anticoagulant (*7*). The concentrations of warfarin required to inhibit the release of factor VII were also higher than in the previous experiment, 10^{-5} to $10^{-3}M$ compared to 10^{-9} to $10^{-6}M$, and at these higher concentrations of warfarin protein synthesis was inhibited. Thus, in slices from animals pretreated with warfarin, the warfarin inhibited response to vitamin K_1 only at concentrations that also inhibited protein synthesis, as measured by incorporation of ^{14}C-L-leucine.

According to the proposed explana-