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Cryotropic gelation of poly(vinyl alcohol) solutions

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Abstract. The mechanisms of the cryotropic gelation of poly(vinyl alcohol) solutions as well as the influence of the characteristics of the polymer and the conditions of the cryogenic treatment on the structure and physicochemical properties of the cryogels obtained are examined. Data on the characteristics of the freezing of concentrated poly(vinyl alcohol) solutions are presented. The influence of soluble additives, possessing different lyotropic properties, on the course of gelation in frozen systems is discussed. The possibility of the cryocracking of poly(vinyl alcohol) chains is considered. The bibliography includes 349 references.

I. Introduction

The cryogels based on polymer systems are macroporous heterophase gels formed as a result of the freezing, storage in the frozen state, and subsequent thawing of the initial solutions or colloidally disperse objects (colloid solutions, pastes, coagulates, *etc*.) in which preconditions for structure formation and transition into a gel are already present or are specially created (for example, by the introduction of a cross-linking agent). An obligatory condition for the formation of heterogeneous gels is then the crystallisation (freezing) of the main bulk of the low-molecular liquid (solvent). After its thawing out, anisotropic macroporous gel-like polymeric products, called cryogels, or cryostructurates are formed.[1–4] As in the case of the usual gels, produced in a liquid solvent, the junctions of the three-dimensional network of the cryogels can be of different nature: they can be established covalently (chemically cross-linked preparations), maintained as a result of relatively undissociated salt or coordinate-ionic bonds (ionotropic systems), stabilised by noncovalent interaction forces [thermoreversible (physical) cryogels], or they may represent a combination of these types of intermolecular contacts.[4–9]

Although individual examples of the formation of gel-like structurates after the freezing – thawing of solutions or dispersions of polymers have been known for a fairly long time (thus sponges produced by the freezing of starch paste were manufactured in Germany in the 1940s [10]), this type of gelation began to be studied systematically only during the last 15 years. These investigations led to the creation of definite ideas about the principal mechanisms of the cryotropic gelation processes, specific effects characteristic of this process alone, its common features with gelation in unfrozen systems, and also the influence of various parameters of each stage of the cryogenic treatment on the properties of the materials obtained.[2, 4–9, 11, 12]

The cryotropic gelation of solutions of poly(vinyl alcohol) (PVA) is examined in the present review. PVA-based cryogels are of great interest — both theoretical and applied. They have found extensive application in biotechnology, medicine, food industry, *etc*. In many respects, this interest is due to the excellent mechanical, diffusional, and thermophysical properties of the PVA cryogels (cryoPVAG), the availability of the polymer itself, its nontoxicity and biocompatibility, and also the relative ease of the method of formation of the gel (the PVA solution is simply frozen for a certain period and then thawed out). By varying the characteristics of the polymer employed (molecular mass, molecular mass distribution, the content of residual *O*-acyl groups, tacticity, PVA concentration in the system) the composition of the solvent, the nature of soluble additives (if these are introduced in the initial system), and also the regime in the cryogenic treatment (temperature and duration of freezing, rate of thawing, the number of refreezing cycles, *etc*.), it is possible to regulate within wide limits the physicochemical parameters of the final gels and their macro- and micro-structures. All these aspects will be discussed in the subsequent sections of the review.

The ability of PVA to give rise to gels after the freezing – thawing of its solutions (here and henceforth we are dealing mainly with a polymer having an insignificant content of acyl residues in the lateral chains) was apparently first observed by Inoue.[13–17] He described the preparation of gel fishing baits from a mixture of a solution of PVA with fillers and aromatising agents. In order to obtain the gel, the initial suspension, poured into an appropriate mould, was initially frozen at a temperature below -5 °C for several tens of hours and then thawed out. In the scientific literature, a direct indication of such gelation appeared in the paper of Kukharchik and Baramboim,[18] who noted that in the case of PVA (M = 80 000) solutions with a concentration > 3 g/100 ml the cryolytic cycles (freezing for 2 min at -78 °C and thawing at 25 °C for 15 min) resulted not only in an increase in viscosity but also in gelation. However, none of the characteristic features of such gelation of PVA and the properties of the cryogels were reported in the above investigation.[18]

Mention should also be made of the work of Polish investigators,[19, 20] who observed by the light scattering method the promoting effect of the cryogenic treatment on the association of

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PVA macromolecules in aqueous media, and also of the somewhat later study by Peppas.[21]

Some time later, the PVA cryogels were, as it were, 'rediscovered'. This is probably associated with the observation of the possibility of increasing the mechanical strength of cryoPVAG as a result of the repeated freezing–thawing of the cryogel already obtained [12, 22–31] or the partial dehydration of the frozen specimen *in vacuo* (partial lyophilisation).[32–40]

According to *Chemical Abstracts*, about 500 communications have been published on the cryotropic gelation of PVA, only a small proportion of these publications having been considered in the reviews of Nambu [11] (1990) and Peppas and Stauffer [12] (1991), as well as in our earlier review [41] (1992). The aim of the present review is to provide a more comprehensive pattern of the state of research into the given problem and also to note the problems which are still obscure.

II. Characteristic features of the freezing of poly(vinyl alcohol) solutions

It is well known that prolonged storage of concentrated aqueous PVA solutions at room temperature gives rise to gel formation (see, for example, Refs 42–46). A similar result can be achieved faster by cooling the system (without freezing) [20, 47] or by impairing the thermodynamic quality of the solvent as a result of the introduction of nonsolvent additives.[48–52] In all cases low-melting (melting point $T_m < 30–40$ °C), mechanically weak, and as a rule almost transparent (opalescent) thermoreversible hydrogels are formed. On the other hand, if concentrated aqueous PVA solutions are initially frozen and are then thawed out after being maintained in the frozen state for a time, then turbid, elastic, high-melting ($T_m > 60–80$ °C) heterogeneous gels (cryogels) are formed under certain conditions instead of the transparent hydrogels. Evidently the behaviour of the water–PVA system subjected to cryogenic action should affect the properties of the cryogels obtained and the kinetics of their formation.

Figure 1 presents a generalised picture of the variation of the temperature of the system at all the stages of cryostructuration, *i.e* on freezing, storage in the frozen state, and thawing. Interval $A–B$ corresponds to the cooling of the specimen from the initial temperature to the temperature of the onset of crystallisation of the solvent (supercooling to a temperature T_u is frequently observed for PVA solutions). Owing to the evolution of the latent heat of crystallisation of ice, a 'crystallisation plateau' is usually recorded along section $C–B$, but at high rates of cooling ($v_c > 40$ K min^{-1}) this plateau may not in fact be observed on the real time scale.[53] A further decrease in temperature occurs between the points D and E up to the experimentally specified value (T_s).

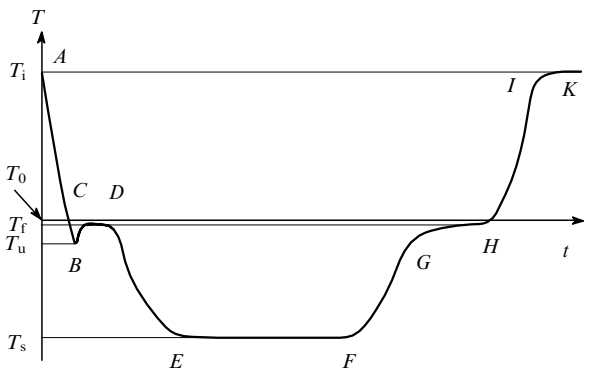


Figure 1. Generalised thermogram for cryotropic gel formation; T_i = initial temperature of the system, T_0 = temperature at which the pure solvent is frozen, T_f = temperature at which the system is frozen, T_u = lowest supercooling temperature, T_s = temperature at which the specimen is stored in the frozen state.

It has been shown [4, 54, 55] that the depression of the crystallisation temperature of the system ($T_0 – T_f$) for 5%–10% aqueous solutions of PVA did not exceed 0.3–0.8 °C, while the extent of supercooling is a parameter poorly reproducible with respect to temperature in view of the statistical nature of the ice nucleation processes.[56] In the main, the trend is as follows: with increase in the PVA concentration in the initial solution, the supercooling temperature (T_u) falls and ice formation proper proceeds at a higher rate. The higher the rate of crystallisation, the finer are the polycrystals of the freezing low-molecular liquid produced.[57] Thus the size of the ice crystals in the 7% PVA solution frozen at −10 °C is several times smaller, and in the 14% solution — smaller by 1–2 orders of magnitude than in frozen pure water.[58]

Such microstructure of the polymer-reinforced ice affects significantly the physicomechanical characteristics of the frozen specimens [59] and an appreciable strengthening of such composite ice is observed even for a 1% PVA content in the initial solution and the ultimate uniaxial compression strength of the 10% preparation frozen at −10 °C is already an order of magnitude higher than for pure ice. After a time, this parameter slowly increases, which has been shown by studies involving the use of the NMR method,[58] to be accompanied by a gradual decrease in the amount of unfrozen water.

Important information about the properties of the water–PVA system at various negative temperatures has been provided by the study of the ESR spectra of a spin probe (4-hydroxy-2,2,6,6-tetramethylpiperidine-1-oxyl) introduced into the initial polymer solution before freezing. It has been found [60–63] that the correlation times of the rotational mobility of the stable nitroxyl radical, which depend directly on the viscosity of the microenvironment where reorientation movements of the probe take place, corresponds, for not unduly deeply frozen PVA solutions, to the rotations of the nitroxyl radical in a highly viscous but liquid medium. This shows that such polymer solutions, solidified by freezing (in particular aqueous PVA solutions), represent at least two-phase systems incorporating the crystalline phase of the frozen solvent and the phase comprising a heavily concentrated polymer solution — the so-called liquid microphase.[64–66] Quantitative estimates of the volume of such liquid microphases of frozen PVA solutions have been made with the aid of a special method [60] for the analysis of ESR spectroscopic data. It has been shown that the amount of the liquid component varies from 0.86–0.88 g of H_2O per gramme of the polymer at −9 °C to 0.75 g of H_2O per gramme of the polymer at −85 °C; the latter quantity was limiting and referred to unfrozen water. Approximately the same result (∼ 0.8–0.9 g of H_2O per gramme of polymer) was obtained with the aid of NMR spectroscopy [67, 68] and differential scanning calorimetry.[69] Taking into account the 10%–15% error of the determination by each of these methods, such agreement should be regarded as rather good.

In the region of 'high' negative temperatures (from −1 to −7 °C), hysteresis phenomena are observed (Fig. 2), *i.e*. the amount of the liquid microphase and hence the concentration of the polymer dissolved in it depend greatly on the thermal prehistory of the system in the real (far from equilibrium) cooling or heating regimes. In particular, if fairly rapid heating of the frozen specimen is arrested at some intermediate temperature (in Fig. 2, this is −4 °C), the system gradually relaxes to a phase state closer to equilibrium (transition *3*, Fig. 2). Therefore, the slower the cooling of the frozen preparation or correspondingly the slower its heating during thawing, the greater is the extent to which the possible transformations of liquid water into ice are able to occur or, conversely, the closer to equilibrium is the amount of the liquid microphase.

Direct observations at negative temperatures of the mobility of the unfrozen part of water in the water–PVA system have been carried out [67, 68] with the aid of ^{2}H NMR spectroscopy. For this purpose, the polymer was dissolved in D_2O. The NMR signals of

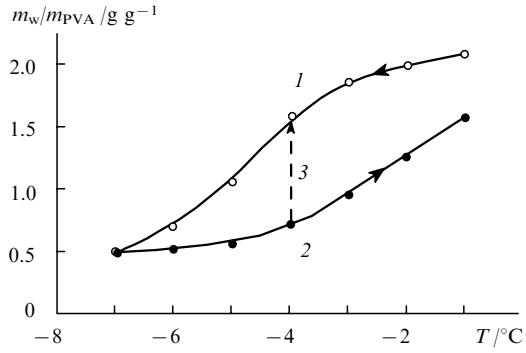


Figure 2. Dependence of the relative amount of unfrozen water on the temperature of the frozen 10% PVA solution (m_w = mass of water remaining liquid in the frozen specimen; m_{PVA} = mass of PVA dissolved in the liquid microphase);[60]
(*1*) cooling of the specimen beyond the crystallisation plateau of pure water; (*2*) heating; (*3*) thermostatic regime at −4 °C.

the heavy water deuterons in the solid and liquid states differ in width by two orders of magnitude and it is therefore possible to record the spectra referring to the D_2O molecules not incorporated in the ice structure. The ^2H NMR spectra of a 10% solution of PVA (M – 82 000), frozen to a temperature of −52.2 °C, which is 56 °C lower than the crystallisation point of the pure solvent (T_0 = + 3.8 °C), contain one symmetrical signal without quadrupole splitting. The width of this signal depends on the temperature and in the temperature range indicated varies from several tens to ∼ 5000 Hz. The nature of the spectra then indicates the virtually isotropic reorientation of the solvent molecule, which indicates the rapid (10^{-5} s on the NMR time scale) rotational and translational diffusion of water in the isotropic medium; *i.e.* in the unfrozen liquid microphase the water molecules are subjected to interactions which are virtually equivalent and equally probable in all directions. On the other hand, the proportion of the solvent located near the anisotropic interfaces is, firstly, small and, secondly, it apparently exchanges rapidly with the molecules from the bulk of the liquid inclusions. On further cooling of the specimen to temperatures 60 – 70 °C lower than its freezing point, the symmetrical Gaussian peak (with a width of ∼ 5 kHz at the level of half its height) is transformed into a two-component signal, the upper component of which has been broadened by a factor of 4, while the lower component, the so-called 'pedestal', corresponds to a signal with a greatly increased spin – lattice relaxation time. It has been suggested [67] that this character of the spectrum at the temperatures indicated is caused by the slow exchange of the ^2H nuclei of the solvent and the polymer.

Thus it has been shown that moderately frozen PVA solutions are heterophase objects containing the unfrozen mobile solvent, the minimum amount of which corresponds to the ratio ∼ 4 water molecules for 3 polar chain groups.

Yet another effect which can occur in principle during the freezing of polymer solutions, including aqueous PVA solutions, is cryocracking , *i.e.* the cryogenic mechanical degradation of the chains of high-molecular compounds under the influence of the dynamic stresses arising on crystallisation of the low-molecular solvent. Berlin and coworkers [70–73] were the first to draw attention to the possibility of such mechanochemical transformations of polymers during the freezing – thawing of their solutions. Somewhat later Jellinek and Fok [74] calculated the critical rates of movement of the fronts of the crystallisation of the solvent (v_{cr}) and of the migration of the microstreams of the liquid ahead of the growing faces of the crystals, which are necessary to develop forces sufficient for the disruption of the covalent bonds of the main framework of the carbochain polymers. These calculations were performed for two types of physical action on the macromolecule: (a) impact across the chain fixed (frozen in) at both ends (which is generally speaking an extremely improbable event) and (b) the frictional shear force of the liquid stream ahead of the crystallisation front exerted on the chain fixed at one end. Calculation yielded the following values of v_{cr}: ∼ 100 m s^{-1} in the first case and ∼ 0.5 m s^{-1} in the second. On the other hand, in practice the attainable rates for preparations with a volume of several millilitres do not exceed 0.002 – 0.003 m s^{-1}.[75] For preparations with a volume of several microlitres, it is possible to achieve an increase in the rate by 1 – 2 orders of magnitude during their rapid freezing (for example, in liquid nitrogen), but even such increase in the rate makes it possible merely to approach the second case. Therefore one should apparently not expect a real manifestation of the mechanical degradation of PVA for shallow freezing of its solution under the conditions employed for the formation of cryoPVAG.

Thus in a study of the behaviour of PVA solutions during thawing and freezing with the aid of capillary viscometry, Kukharchik and Baramboim [18, 76] failed to observe any kind of cracking of PVA either during single or repeated freezing – thawing of dilute and semidilute solutions of the polymer (M = 80 000). Nevertheless, facts have been described which indicate, according to the authors,[77–80] the occurrence of homolytic cleavage of PVA by the cryogenic influence; here it has also been suggested [77] that cracking is accompanied by the simultaneous covalent cross-linking of the polymer molecules as a result of reactions between the macroradicals formed and the neighbouring chains.

However, a thorough test of the results of the above studies [77–80] failed to confirm the conclusions reached in them.[81, 82] In the first place, the cryoPVAG are thermoreversible gels which melt on heating (for example, on a boiling water bath). Here the viscosities of the initial solutions of PVA (c_p = 6% – 10%) having different molecular masses (69 000 – 110 000) and solutions obtained from the corresponding cryogels after fusion of the latter hardly differ, which indicates the absence of intermolecular cross-linking. Capillary viscometry does not reveal reliably detectable changes in the intrinsic viscosities of the PVA preparations, provided that the initial polymer does not contain any impurities. Thus lines *4* and *5* in Fig. 3 illustrate the dependence of [η] on the number of cycles in the cryogenic treatment of solutions of two different batches of the same brand of technical-grade PVA, for which both a decrease (line *5*) and an increase (line *4*) in [η] were observed, whereas variation within wide limits of the freezing – thawing regimes for solutions of the same polymer purified by reprecipitation does not induce changes in the intrinsic viscosity (lines *1* – *3*, Fig. 3). Thus the possible reactive impurities contained in industrial PVA, concentrated in the liquid microphase of the frozen preparations, may be the cause of the change in the properties of the polymer recorded after the cryogenic action.

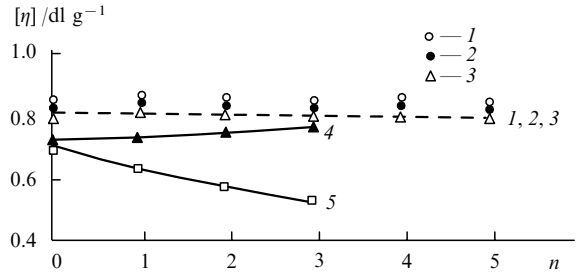


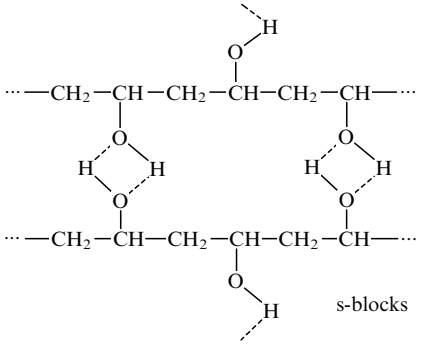
Figure 3. Dependence of the intrinsic viscosity [η] of PVA on the number of freezing – thawing cycles (n) for a 10% PVA solution of brand 20/1.
(*1*) – (*3*) PVA purified by reprecipitation (M = 81 700, DD = 98%); (*4*) and (*5*) unpurified PVA (two different batches of technical-grade polymer). Cryogenic treatment regimes: (*1*), (*4*), and (*5*) v_c = 1.8 K min^{-1} (freezing at −15 °C and storage at this temperature for 18 h), heating rate v_{th} = 1.0 K min^{-1}; (*2*) v_c = 1.8 K min^{-1}, v_{th} = 0.3 K min^{-1}; (*3*) v_{th} = 180 K min^{-1} (freezing in liquid nitrogen for 30 min and storage at −15 °C for 18 h), v_{th} = 0.3 K min^{-1}.

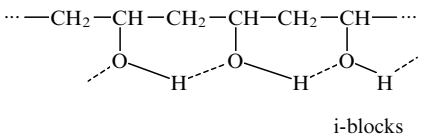
What precisely these impurities are is unknown, their compositions and amounts are not the same in different batches of the polymer of the same brand. On the other hand, in the case of specimens of pure PVA the changes in molecular mass and manifestations of mechanical degradation are not observed either viscometrically or with the aid of high performance GPC or any other physicochemical methods — IR, ESR, *etc*.[81,82] One may therefore conclude, to within the sensitivity of the analytical procedures employed, that the cracking of the PVA chains on cryogenic treatment is negligible, if it does occur at all, which is in no way reflected in the cryotropic gelation of the given polymer.

III. Dependence of the properties of poly(vinyl alcohol) cryogels on the characteristics of the gel forming polymer

The structure and properties of PVA cryogels depend on many factors, including both the characteristics of the polymer itself and the conditions of the low-temperature gelation. One of the most important parameters determining the possibility, in principle, of the formation of cryoPVAG, is the presence in the polymer of residual *O*-acetyl groups.[9,24,25,83] In the majority of cases described, the cryogels were prepared from poly(vinyl alcohols) obtained by hydrolysing poly(vinyl acetate). It was found that, for a degree of deacetylation (DD) below 90%, the cryoPVAG are not formed under any, even the most favourable, conditions. For a content of OAc residues of 5%, very weak cryogels are obtained, and it is actually difficult to measure correctly their rheological characteristics. Only on the basis of concentrated aqueous solutions of PVA of highly deacylated brands (DD > 97%) is it possible to form fairly strong cryogels. Bearing in mind that the bonds between the polymer chains in the gels formed are noncovalent, *i.e*. the intermolecular contacts in the regions of microcrystallinity are ensured by a multiplicity of hydrogen bonds between the secondary alcohol groups of different chains,[35,84] the steric hindrance generated by the bulky OAc residues, interfering with the establishment of extended complementary contacts, should be included among the evident causes of the 'poor' gelation of the insufficiently deacylated PVA preparations.

The macromolecules of atactic poly(vinyl alcohols) in water are known[43,85,86] to tend to associate, whereupon the intermolecular hydrogen bonds arise mainly with participation of the OH groups of the syndiotactic (s) PVA blocks while the intramolecular hydrogen bonds are produced with participation of the OH groups of the isotactic (i) fragments.





Thus the higher the content of the s-diads in the polymer employed, the stronger is the manifestation of the tendency towards phase separation in its solutions[87,88] with formation of a microgel fraction, a gel, or even a precipitate. The cryogels based on PVA enriched in syndiotactic fragments have a higher degree of crystallinity[89] compared with specimens based on the atactic polymer of approximately the same molecular mass, which indicates the retention of the above tendency also on cryotropic gelation of this polymer. Unfortunately the cryoPVAG prepared from poly(vinyl alcohols) with an increased content of s-sections have been inadequately investigated, but there is no doubt of the interest in such studies, particularly since new ways of synthesising PVA with a controllable tacticity are being vigorously developed nowadays.

It is entirely evident that the molecular mass of the polymer used for the formation of cryogels must influence its properties. Thus fairly weak cryoPVAG are obtained from highly concentrated (c_p = 20%) solutions of PVA with a low degree of polymerisation (M < 30 000–40 000),[4,11,24,54,90] so that it is preferable to employ PVA brands with M > 50 000 for the formation of strong cryogels.

Figure 4 presents the creep curves for equiconcentrated cryoPVAG prepared from PVA with different contents of the residual OAc groups and different degrees of polymerisation. For the close molecular masses (curves *2* and *4*), the additional presence in the polymer of even small amounts (1.3%) of unhydrolysed side groups affords a cryogel with a compliance greater by a factor of 3, whilst in specimens with an almost identical degree of deacylation of PVA (curves *1*, *2*, and *3*) less compliant (more elastic) cryoPVAG are obtained for the higher the molecular mass of the polymer.[54] These and similar results[4,24,25,90–93] for the influence of the size of the PVA macromolecules on different characteristics of the corresponding cryogels are fully consistent with the well-known dependences of the properties of noncovalent thermoreversible gels (formed at positive temperatures) based on both PVA[49,94–97] and other polymers.[98–101] Since the hydrodynamic dimensions of the macromolecules increase with increase in the chain length, the degree of overlap of the coils in solution rises and the number of topological entanglements increases, *i.e*. there is an increase in the number of intermolecular contacts, as a result of which a denser physical network is produced in the gel formed. Such gels are harder and have higher melting points

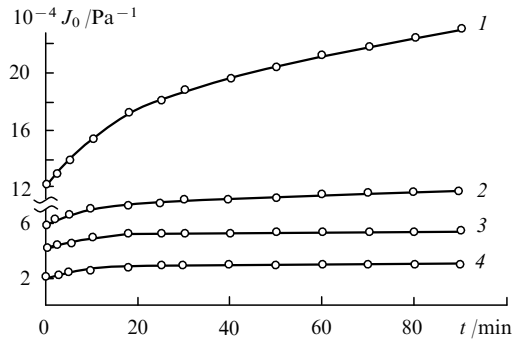


Figure 4. Creep curves for cryogels formed from 10% aqueous solutions of PVA with different molecular masses and degrees of deacylation.[54,91] (*1*) M = 69 000, DD = 98%; (*2*) M = 90 000, DD = 98%; (*3*) M = 110 000, DD = 98%, (*4*) M = 95 000, DD = 99.3%. Cryostructuration regime: T_s = −10 °C, t_s = 24 h, υ_{th} = 1.0 K min^{-1}.

The properties of cryoPVAG are influenced similarly also by the variation of the PVA concentration in the initial solution — the higher the concentration, the stronger and more thermostable (other conditions being equal) are the corresponding cryogels obtained.[4,9,11,12,22–25,35–37,40,54,55,58,83,84,89,91,102–113] It is shown in Fig. 5 that the cryogel formed on cryotreatment of a 10% PVA solution is fairly compliant and is deformed appreciably during the application of a shear load, whereas the cryogels obtained from a 14% and especially a 16% PVA solution exhibit only a slight creep under the same shear stresses.

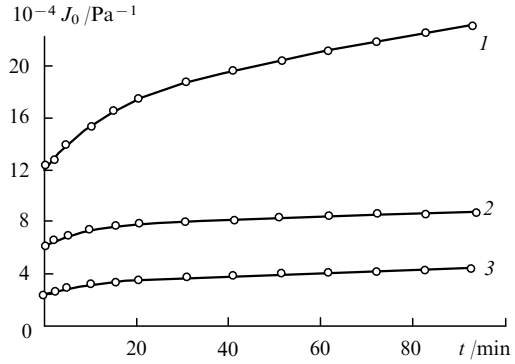


Figure 5. Creep curves for cryogels formed from aqueous solutions of PVA (M = 69 000, DD = 98%) with different polymer contents: (*1*) 10%; (*2*) 14%; (*3*) 16%.[91] Cryostructuration regime: $T_s = -10$ °C, t_s = 24 h, υ_{th} = 1.0 K min^{-1}.

When a PVA solution freezes, the pure solvent crystallises initially (Fig. 1), while the solute is concentrated in the still liquid part of the specimen. Such cryoconcentration intensifies significantly the polymer–polymer interactions which ultimately leads to the formation of stable junction of the three-dimensional cryogel network. Since these processes occur in a heterophase system, a heterogeneous gel is obtained after it has thawed out. Pores of different size and geometry are formed in it under the influence of the crystals of the frozen solvent. Thus the solvent plays the role of a porogen. According to electron microscopy data, the structures of the cryoPVAG formed from solutions with unequal polymer contents differ, although their structural feature such as pronounced heterogeneity, *i.e.* the presence of micropores and macropores, is characteristic of any PVA cryogels. The morphology of 14% and 16% cryoPVAG is illustrated in the photomicrographs in Figs 6*a* and 6*b*. Their creep curves are presented in Fig. 5 (curves *2* and *3*). The high porosity of the preparations is most striking. With increase in the PVA concentration, a decrease in the size of the macropores and a thickening of the elements of the polymer phase of the heterogeneous gel are observed, which agrees well with the smaller compliance of the more concentrated specimen.

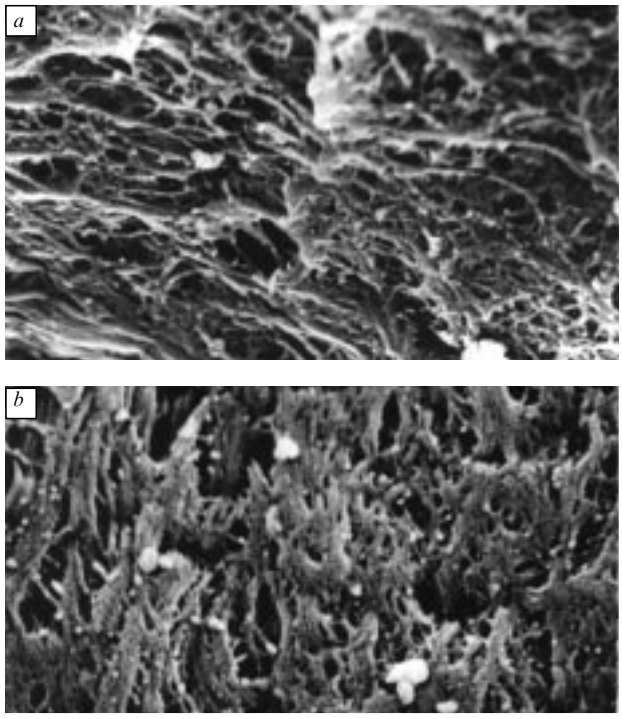


Figure 6. Structures of cryogels formed from 14% (*a*) and 16% (*b*) aqueous solutions of PVA (M = 69 000, DD = 98%).[54,91]
Cryostructuration regime: $T_s = -10$ °C, t_s = 24 h, υ_{th} = 1.0 K min^{-1}.

Perhaps the only characteristic of PVA the influence of which on the properties of cryoPVAG has so far been virtually uninvestigated is the molecular mass distribution (MMD) of the gel forming polymer. Nevertheless it is quite evident that the use of PVA with a narrower MMD should promote an increase in the strength parameters of the cryogels.

IV. The influence of the conditions in the cryogenic treatment on the properties of poly(vinyl alcohol) cryogels

It was already stated above that virtually all the parameters of the regimes in the cryogenic treatment influence, albeit not to the same extent, the characteristics of the cryoPVAG and the dynamics of their formation. These questions have been investigated in fair detail.

The process temperature and the effectiveness of the heat exchange determine the possibility of the supercooling and the rate of crystallisation of the specific specimen: usually the lower the T_f (Fig. 1), the lower the probability of the supercooling, and hence the more rapid the liquid–solid phase transition for the main bulk of the low-molecular solvent. By altering the thermal conductivity conditions (for example, by employing vessels made from different materials, or by increasing the thickness of the walls of the vessel, or by employing thermal insulation), it is possible to control the dynamic freezing and thawing parameters. As a result of such experiments, it has been found[55,102] that the degree of supercooling and the rate of crystallisation of ice do not vary in parallel with the variation of the rate of cooling, which indicates the complexity of the dependence of the freezing regimes for concentrated aqueous PVA solutions on different process factors. Thus, for a 14% polymer solution poured into a 5 mm duralumin mould, the change in υ_c from 0.09 to 17.0 K min^{-1} (*i.e.* almost by a factor of 190) entails a change in υ_{cr} in the range from 0.35 to 2.5 K min^{-1} (the difference is a factor of only 7.1), while the rheological parameters of the cryogels obtained altogether change very slightly and, other conditions being equal, depend little on υ_c. Therefore, in comparing the properties of the cryoPVAG specimens formed at different T_f, the influence of the dynamics of the freezing itself may be virtually disregarded. In the main, the physical characteristics and the structure of the PVA cryogels are determined by the temperature and duration of the cryogenic action,[24,58,91,106,114] provided that the preparations are thawed out under identical conditions.[55,115] Thus it has been observed that, after brief (up to 24 h) storage of the specimen in the frozen state, the lower the T_f, the less compliant the corresponding cryoPVAG. With increase in the duration of the cryogenic process, the trend changes (Fig. 7). The specimens kept at -20 °C and then for 24 h at -10 °C become harder than the preparations maintained at -30 °C. A characteristic feature is that the duration of the storage in the frozen state ceases to influence their strength properties fairly early (after $\sim$24 h), whereas in the specimens stored at -10 and -20 °C the values of J_0 after cryogenic treatment for 10 days still remain unstabilised,[91] which indicates the continuation at these temperatures of the changes associated, as already mentioned, with the slow decrease in the amount of the uncrystallised solvent.[58]

Like their strength, the thermophysical properties of the cryoPVAG also depend on the parameters examined above; the increase in the degree of deacylation or in the molecular mass of the polymer as well as in its concentration in the initial solution promotes an increase in the melting point of these thermoreversible gels.[11,23–25,35–37,40,54,55,83,105,106] A decrease in T_f and an increase in the duration of the storage of the specimens in the frozen state exert the same influence.[55,106]

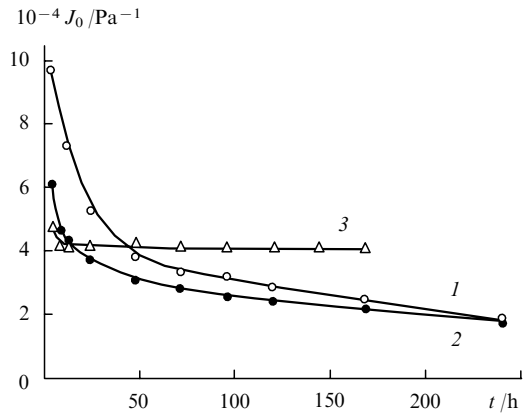


Figure 7. The influence of the temperature and duration of freezing of 14% solutions of PVA (M = 69 000, DD = 98%) on the rheological properties of the cryogels formed.[91]
T_s (°C): (*1*) −10; (*2*) −20; (*3*) −30.

However, the most significant factors which radically affect the properties of the PVA cryogels are the regimes of the defrosting of the specimens.[55, 106, 109, 115, 116] A detailed study of this stage of the cryostructure formation made it possible to establish the principal features of the mechanisms of this type of gel formation. It has been observed [4, 54, 55] that, when the thawing out is carried out at a rate greater than 10 K min^{-1}, then, regardless of the conditions under which the initial polymer solution was frozen and then exposed to temperatures between −10 and −30 °C, one obtains after such 'rapid' thawing out not a gel but a viscous and turbid colloid solution. Conversely, on slow thawing out ($v_{th} \leqslant 0.05-0.01$ K min^{-1}) very elastic cryogels are formed.

Figure 8*a* illustrates the influence of the rate of thawing of the specimens on the apparent instantaneous compliances (J_0) of the PVA cryogels, whilst Fig. 8*b* demonstrates the dependence of the same rheological parameter on the polymer concentration in the initial solution for two series of experiments in which the thawing out was carried out at rates of 1.0 and 0.02 K min^{-1}.

Figure 8 shows that the compliance of the cryogels diminishes as the thawing out of the corresponding preparations slows down; for v_{th} = 1.0, 0.1, and 0.02 K min^{-1}, $J_0 = 8.1\times10^{-4}$, 0.6×10^{-4}, and 0.45×10^{-4} Pa^{-1} respectively (Fig. 8*a*). If the PVA solution is maintained at −20 °C for 10 days and is then thawed out at a rate of 1.0 K min^{-1}, then a cryogel with $J_0 = 1.25\times10^{-4}$ Pa^{-1} is obtained, while in the case where the rate of thawing is lower by an order of magnitude (v_{th} = 0.1 K min^{-1}), after freezing for 1 h at

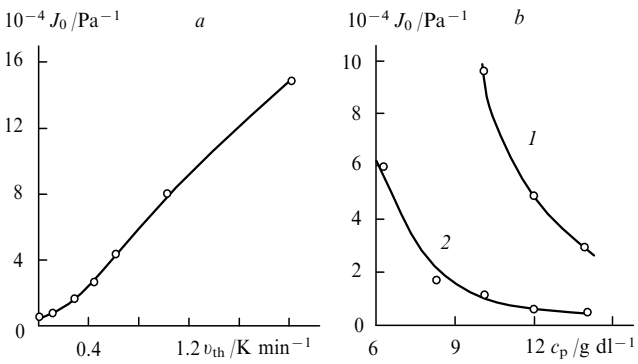


Figure 8. The influence of the rate of thawing of the specimen (*a*) and of the concentration of the polymer in the initial solution (*b*) on the rheological properties of cryogels formed from aqueous solutions of PVA (M = 69 000, DD = 98%).[55]
(*a*) c_p = 14%; (*b*) T_s = −20 °C, t_s = 1 h, v_{th} = 1.0 (*1*) and 0.02 K min^{-1} (*2*).

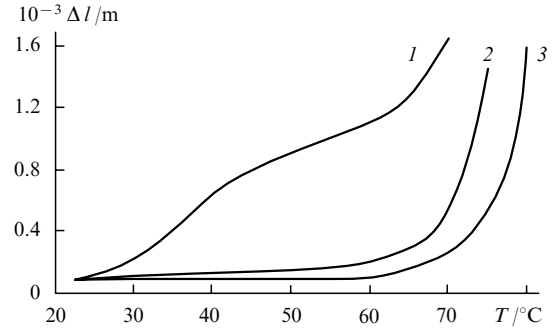


Figure 9. Thermomechanical properties of cryogels formed from 14% solutions of PVA (M = 69 000, DD = 98%) at T_s = −20 °C and t_s = 1 h and thawed out at different rates v_{th} (K min^{-1}):[106] (*1*) 1.0; (*2*) 0.2; (*3*) 0.02.

−20 °C a more rigid cryoPVAG is formed. Similarly a decrease in v_{th} makes it possible to lower the concentration of the gel forming agent without loss of the strength characteristics of the cryoPVAG (Fig. 8*b*).

Figure 9 presents the thermomechanical curves for specimens of cryogels thawed out at different rates. It is seen from the figure that the slowly thawed out preparations are, firstly, deformed to a smaller extent by an applied load as the temperature rises and, secondly, they melt at higher temperatures on heating, *i.e.* are more thermostable.[106] The presence of two inflection regions on the thermomechanical curve for the specimen which was thawed out fairly rapidly (curve *1*, Fig. 9) indicates the presence in the structure of such a gel of at least two types of junctions differing in the thermal dissociation energies. Those of the first type melt at 35–45 °C, while these of the second type melt at 60–65 °C. Two endothermic peaks have been recorded in the same temperature ranges also with the aid of differential scanning calorimetry [38, 116] and the first of these, corresponding to the decomposition of the low-melting nodes, is approximately at the temperatures (20–40 °C) at which melt the usual thermoreversible PVA hydrogels formed on ageing of concentrated polymer solutions without freezing.[44, 117] On the other hand, the complete fusion of the cryoPVAG, caused by the thermal dissociation of the high-melting junctions (the microcrystallinity zones), occurs at a temperature higher by tens of degrees. The melting points T_m, like the other characteristics of the gel objects, are sensitive to the previous thermal history of the specimens (Table 1).[55]

If the dependence of the melting point of the cryoPVAG on the polymer concentration in the system is represented in terms of the variables of the Eldridge–Ferry equation [98]

$$\lg c_p = \frac{\Delta H}{2.3RT} + \text{const},$$

Table 1. The influence of the conditions in the cryotropic gel formation on the melting point of cryoPVAG.

Cryogenic treatment regimes			T_m /°C
T_f /°C	t_f /h	v_{th} /K min^{-1}	
−10	24	1.00	73.5 ± 0.3
−20	24	1.00	74.0 ± 0.2
		0.20	74.8 ± 0.2
		0.02	76.0 ± 0.2
	72	1.00	74.1 ± 0.2
	240	1.00	74.4 ± 0.1
−30	24	1.00	73.7 ± 0.2

Note. A 14% solution of PVA with M = 69 000 and DD = 99.0% was used.

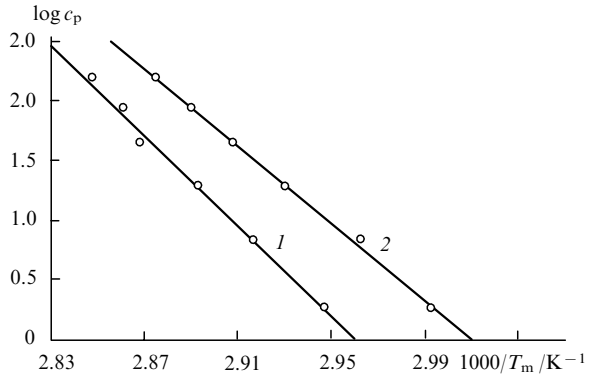


Figure 10. Relation between the melting points of cryogels and the concentration of PVA (M = 69 000, DD = 98%) in the initial solutions frozen at −20 °C during 24 h and thawed out at the rate of 0.02 (*1*) and 1.0 K min^{-1} (*2*)[55] in terms of the variables of the Eldridge–Ferry equation.

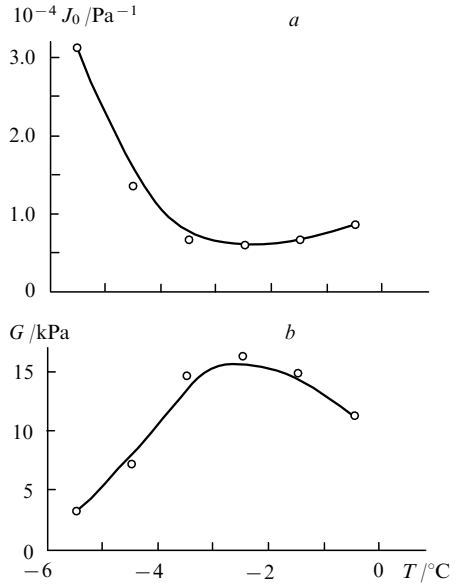


Figure 11. Dependence of the shear compliances (*a*) and the moduli of shear elasticity (*b*) of cryogels formed from 14% solution of PVA (M = 69 000, DD = 98%) on the temperature at which the frozen specimens were maintained in the subzero region.[4, 55]

it is possible to estimate the enthalpies of fusion of the cryogels obtained under different conditions (Fig. 10). The values of ΔH are 68 ± 2 kJ mol^{-1} for preparations thawed out at a rate of 1.0 K min^{-1} and 87 ± 2 kJ mol^{-1} for preparations thawed out at υ_{th} = 0.02 K min^{-1}.[55] Comparison of these quantities with the available data[44] for the usual PVA hydrogels obtained on ageing of 10%–20% solutions of the polymer (M = 60 000), the melting points of which are in the range 14–28 °C and ΔH = 37 kJ mol^{-1}, shows clearly that the energy of the thermal decomposition of the junctions of the cryogel network is at least twice as high as for the usual gel, *i.e.* the promoting effect of the freezing of the PVA solutions on the association of the macromolecules of the polymer and its crystallisation is clearly seen.

The microstructure of the PVA cryogels also depends on the dynamics of the thawing out process: the slower is the thawing out process, the lower the degree of heterogeneity of the preparations according to scanning electron microscopy data.[4, 54, 55, 118] According to transmission electron microscopy data,[91] the primary elements of the supermolecular structure of the cryoPVAG are globular formations 0.01–0.02 μm in diameter, combined into larger globular aggregates 0.2–0.5 μm in diameter, which form in their turn bead-like strands of the three dimensional network of the macroporous cryogel. It is of interest that similar globular aggregates have been observed[51] also in the structure of hydrogels obtained either on ageing of concentrated polymer solutions or after the introduction of a nonsolvent.

The following question is relevant: if the rate of freezing of the polymer solutions influences little the properties of the cryoPVAG, the temperature and the time of the cryogenic treatment exert a definite effect on the characteristics of the cryogels, and the dynamics of the thawing out process is of decisive importance for them, then what is the precise stage in the cryostructure formation process where gelation proper takes place — during freezing (where the polymer is concentrated in the liquid microphase as a result of the crystallisation of ice), during the storage of the frozen solutions at a negative temperature, or in the course of the thawing out process?

It has been shown[55] that, when the PVA solution is initially frozen at −20 °C for 1 h, is subsequently maintained at a temperature in the range from −0.5 to −6.0 °C, and is then rapidly (in order to rule out the influence of the thawing out dynamics) thawed out, the dependence of the rheological characteristics of the cryogels formed by means of this scheme on the temperature at which they are stored has an extremum (Fig. 11). The least compliant (Fig. 11*a*), *i.e.* the most elastic, cryoPVAG is formed when the frozen system is maintained in the region of −2.5 °C (Fig. 11*b*): above and below this temperature, less strong cryogels are obtained. On the other hand, overall the region of the maximum effectiveness of such cryotropic gel formation is in the subzero temperature range — only several degrees below the crystallisation point of the solvent.

Hence the influence of the thawing out kinetics on the properties of the PVA cryogels becomes understandable: the slower and closer to equilibrium conditions is the thawing out of the specimen, the longer it resides in the region of temperatures optimum for the formation of the gel network. For example, on rapid thawing (υ_{th} = 10 K min^{-1}) the system 'passes' through the range −5–0 °C in only 30 s, in the moderate thawing out regime (υ_{th} = 0.1 K min^{-1}) the passage takes 5 min, while in the slow regime (υ_{th} = 0.02–0.01 K min^{-1}) the passage takes 4–8 h. Thus a slow increase in temperature during thawing out is in a certain sense equivalent to the storing of the frozen preparations for a long time at the temperatures corresponding to the formation of the strongest cryogels, when in the PVA–water system mainly the junctions of the three dimensional network of the cryoPVAG are formed. If the concentrated aqueous solutions of the polymer during their cooling to the temperatures of the most intense gelation (∼−2.5 °C) could be guaranteed to freeze, which is frequently prevented by supercooling effects, then in this case there would apparently be no need at all for the use of lower temperatures. In fact they are required to induce the crystallisation of ice.

It has been demonstrated with the aid of NMR spectroscopy[67, 68] that when the frozen preparations are heated after the attainment of a threshold temperature range, which is 4–6 K below the crystallisation point of the system, a sharp increase in the amount of the mobile solvent is observed. An additional amount of the liquid component appears precisely at these temperatures still in the solid frozen specimen in addition to the firmly bound unfreezable solvent (see also Fig. 2). By virtue of the partial 'prefusion' of the ice, a medium is produced in which the macromolecules (or their segments) acquire a certain mobility, which ultimately leads to effective polymer–polymer interactions with formation of microcrystallites performing the function of cryogel network junction knots.

It is shown in Fig. 12 that such mobility is reflected in the ^{13}C NMR spectra of the PVA–water system, while the signals of the CH(OH) and CH_2 groups of PVA are detected at 66 and 44 ppm respectively. Since the polymer is dissolved in D_2O in order to record the spectra, the temperature scale on the figure is

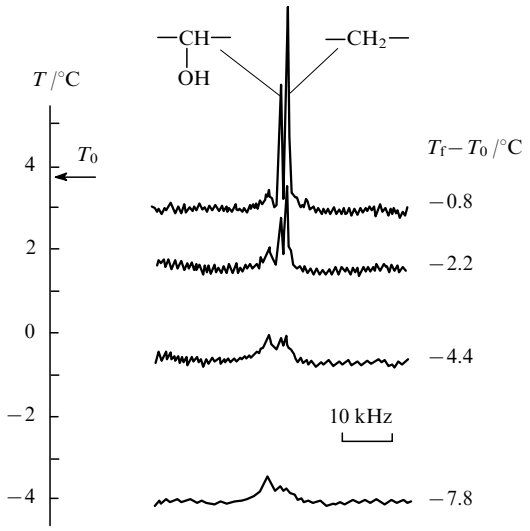


Figure 12. ^{13}C NMR spectra of a 10% solution of PVA (M = 81 700, DD = 98%) in D_2O frozen at −20 °C and then maintained for 2 h at the temperature of the recording of the spectrum.[67]

indicated both in absolute numbers and relative ($T_f - T_0$) to the melting point of the pure solvent.

At $T_f - T_0 = -7.8$ °C, the resonance peaks of the carbon atoms of PVA are hardly noticeable, while at a temperature three degrees higher, at $T_f - T_0 = -4.4$ °C, fully resolvable, although weak, signals are already observed. On further increase in temperature, but still 2–3 °C below the temperature of the thawing out of the specimen as a whole, the 'normal' spectrum of the polymer solution in D_2O is recorded. Hence it follows that, in the temperature range 5–6 °C below the freezing point of the system, there is a conventional boundary of the retardation of rapid (on the NMR frequency scale) movements of the carbochain framework of PVA. Estimation of the correlation times of the spin–lattice relaxation of the polymer carbon atoms, which serves as a criterion of the mobility of the kinetic segments of the chain, shows that the reorientation movements of the ^{13}C nuclei of the CH_2 groups of PVA in the system frozen at subzero temperatures occur more slowly by two orders of magnitude than in the initial liquid solution. It is precisely because of the low mobility of the polymer chains that a fairly prolonged time is needed for the occurrence of the cryotropic gel formation. The passage through an extremum of the dependence of the rheological properties of the cryoPVAG on the temperature of the cryotropic structuration process in its subzero region then becomes understandable (Fig. 11). On the one hand, at temperatures above the extremum there is a significant increase in the amount of the mobile solvent, *i.e.* the specific concentration of the gel forming agent is reduced in the liquid microphase. This entails a decrease in the probability of effective intermolecular contacts, which are also acted against by the intensification of the thermal movement in the system. On the other hand, at temperatures below the extremum there is a rapid decrease in the amount of the 'additional' mobile solvent (the polymer retains only very strongly bound water), *i.e.* the liquid medium in which movements leading to the mutual approach of the interacting sections of neighbouring chains may occur vanishes. Thus, having ensured a prolonged residence of the system in the temperature range −2 to −3 °C after freezing, for example during slow thawing, it is possible to prepare even from solutions with a not very high PVA concentration a cryogel which is several times less compliant than the cryogel obtained from a significantly more concentrated polymer solution but under the conditions of a brief residence of the specimen at subzero temperatures [at $\upsilon_{th} = 0.02$ K min^{-1} for an 8% PVA solution, $J_0 = 1.55 \times 10^{-4}$ Pa^{-1} (Fig. 8*b*), whereas at $\upsilon_{th} = 1.0$ K min^{-1} for a 16% PVA solution, $J_0 = 7.9 \times 10^{-4}$ Pa (Fig.5) for the same freezing time $t_f = 1$ h].

As regards the influence on the properties of the cryoPVAG of cryogenic treatment parameters such as the temperature and duration of freezing (Fig. 7), they are more likely to act on the process involving the formation of a microgel fraction, which then performs the function of building blocks for the formation (in the range of subzero temperatures) of a gel throughout the volume of the specimen. At any rate, the liquid colloidal systems formed were more viscous and turbid the longer the corresponding objects existed in the frozen state.[54] The structure of the supermolecular aggregates entering into the composition of such a microgel fraction has not so far been investigated, although data of this kind would be very useful for the understanding of the nature of the processes under discussion.

Yet another example of the cryogenic treatment which makes it possible to increase the strength characteristics of cryoPVAG is repeated freezing–thawing of the PVA–water system. A large number of communications (see Refs 11, 12, 23–25, 28, 30, 40, 69, 84, 104, 105, 108, 119–134) and patents [22, 26, 27, 29, 135–151] have been devoted to the study of this phenomenon and its employment. Repeated cryogenic treatment ('temperature saw') promotes more far reaching gel formation in these systems. Thus the cryogel obtained as a result of four freezing–thawing cycles for a solution of PVA (M = 75 000 and DD = 99.5%, c_p = 15%, T_f = −20 °C, t_f = 24 h, thawing at 15 °C for 7 h) has a dynamic Young's modulus an order of magnitude greater [30] than that of the specimen obtained as a result of a single cycle. According to X-ray diffraction data,[28, 84] such successive freezing–thawing increases the content of the crystallites and their dimensions in the cryoPVAG. The repeated 'passage' of the system through the region of temperatures corresponding to the most intense gelation both during thawing and freezing (starting from the second cycle for what are no longer solutions but cryogels) leads to the formation of new additional intermolecular contacts and to an increase in the extent of those existing beforehand. In particular, this is manifested by the appearance of numerous compacted regions in the structure of the cryoPVAG observed [84] even under the light microscope. Admittedly the authors [69] do not regard this as the main cause of the increase in the strength of the cryogels, attributing the main role to the intensification of the interactions (hydrogen bonding) between water molecules and the OH groups of the PVA chains with increase in the number of refreezing cycles. However, this conclusion appears controversial. It is more likely that the converse is true: as a result of the crystallisation of PVA, water is displaced from the microcrystallinity zones. It is apparently not permissible to disregard also the compaction of the supermolecular strands of the cryogel network by the purely mechanical mutual approach due to the action of the faces of the ice crystals growing in it. This results in an increase in the strength parameters of the cryoPVAG and an increase in their thermal stability (T_m increases).[40, 105]

Yet another regime in the cryogenic treatment, influencing the characteristics of the PVA cryogels, is the partial sublimation of ice from the frozen specimens. As already mentioned in the Introduction, this method [31–39] makes it possible to increase the mechanical strength of the cryoPVAG, primarily as a result of the increase in the strength of the surface layers of the preparations,[37] because the sublimation of water vapour takes place initially from the peripheral open sections of the frozen block and the crystallised solvent sublimes from increasingly deeper regions only as evacuation proceeds. It has been shown [35–37] that an increase in the duration of such lyophilisation leads to a lowering of the compliance of cryogels in relation to compression, to a decrease in the tangent of the mechanical losses angle following the application of a variable-sign load, and to an increase in the tensile strength of the specimens. According to patent data [31–34, 38, 39, 152–162] the degree of hydration of the frozen PVA solutions subjected to such vacuum treatment can reach > 90%, *i.e.* almost all the nonsolvate water may be removed. On subsequent immersion of the xerogel in an aqueous

medium, it swells slowly, after which the osmotic characteristics of the preparations remain unchanged for a long time.[37]

Thus cryogenic action on the PVA – water system makes it possible to vary within wide limits the properties of the noncovalent cryogels of this polymer and to modify their macroporous structure. Here the dominant factor, determining the effectiveness of the cryotropic gelation of PVA, is the time during which the frozen preparation resides at 'high' negative temperatures.

V. Dependence of the properties of poly(vinyl alcohol) cryogels on the nature and composition of the initial solvent

The previous sections dealt with the influence of the characteristics of the PVA and the freezing — thawing regimes on the cryotropic gel formation and the parameters of the cryogels obtained. Only aqueous solutions of the polymer without appreciable amounts of other components were then considered as the initial objects. However, there is no doubt that the nature of the solvent employed and the presence of various additives should exert a definite effect on the freezing processes of the initial PVA solutions, the volume and composition of the liquid microphases, and the range of optimum temperatures of gel formation (if this occurs), on the one hand, and the properties and texture of the materials produced, on the other.

For example, 10% – 16% solutions of PVA (M = 69 000, DD = 99.0%) in DMSO (T_0 = 18.4 °C) at room temperature remain liquid for a long time, whilst the freezing – thawing of such solutions leads, as for the aqueous solutions, to the formation of cryogels.[9] However, the morphologies of the cryoPVAG obtained from aqueous and dimethyl sulfoxide solutions differ significantly.[107, 163] In particular a layer of an aqueous cryoPVAG 0.6 mm thick (M = 74 800 and DD = 99.5%, c_p = 20%, T_f = −20 °C, t_f = 10 h, thawing for 10 h at 5 °C) transmits about 40% of light at a wavelength of 570 nm, while the same layer of cryoPVAG formed from a solution in DMSO in which the organic solvent has been replaced by water transmits 76% of light, *i.e.* is more transparent.[163] Incidentally, the formation of PVA cryogels from solutions in DMSO itself disproves the hypothesis of Nagura *et al.*,[69] mentioned above, that water molecules are involved in the structure of the tight contacts between the polymer chains on formation of crystallites. The characteristic features of the cryotropic gel formation in the PVA – DMSO system are virtually the same as in the PVA – water system, although the dimensions of the molecules and the physicochemical properties of DMSO and H_2O differ significantly. In the cryogel formed from DMSO, it is possible to replace fully the DMSO by water on prolonged washing. This could hardly be done if DMSO molecules play the role of stable bridges (*via* hydrogen bonds) between the polymer chains.

The cryoprotecting properties of DMSO are well known.[164, 165] The addition of 40% – 80% of DMSO to aqueous systems very greatly reduces the freezing points of the latter. If PVA solutions are prepared in water – DMSO mixtures, they gelate on cooling long before the attainment of the freezing point,[89, 95, 96, 166, 169] affording transparent thermoreversible gels, which after washing out the DMSO can be used for the preparation of soft contact lenses.[166] However, if the DMSO content in the initial system is either below 30 vol.% or above 90 vol.%, the corresponding PVA solutions freeze at −40 °C [107] and after their thawing out macroporous cryogels are obtained (here it is important to employ rapid freezing to ensure that there is sufficient time for the crystallisation of the system before the onset of gelation).

The effects caused by the competition between the rates of freezing and formation of the 'usual' gels have been clearly demonstrated in studies of the cryotropic gelation processes in water – polyol – PVA systems.[170 – 172] When polyols such as glycerol, ethylene glycol, and oligo(ethylene glycol) (OEG) are introduced into aqueous PVA solutions, they lower the critical polymer gelation concentration and increase the temperature of the sol – gel transition as a consequence of the impairment of the thermodynamic quality of the solvent.[48 – 52] However, the gelation process itself in the presence of a not unduly high content of such polyols is fairly slow and, in order to obtain the cryogels, it is therefore necessary to 'accelerate it' kinetically with the aid of rapid freezing. It has been found that the rate of freezing affects the compliance of the cryoPVAG prepared from aqueous solutions of the polymer to which oligomeric ethylene glycols have been added: the slower the freezing of the specimen, the weaker, other conditions being equal, the cryogel obtained.[172] The main cause of the decrease in the strength of such specimens is that on slow cooling the gelation of the system begins before its freezing, as a consequence of which ice crystallises in the bulk of the gel formed, disturbing its structure. On the other hand, on rapid freezing the usual gel has insufficient time to arise and for this reason the mechanisms of the cryotropic gelation occurring in a medium significantly more concentrated in terms of the polymer than the initial solution 'work' subsequently in the frozen heterophase system.

The nature of the influence of the addition of ethylene glycol (EG) and its oligomers on the rheological and thermophysical properties of the corresponding cryoPVAG is illustrated in Fig. 13. An increase in the content of EG in the initial polymer solution leads to less hard and readily fusible cryogels (glycerol and propylene glycol act similarly), but, starting with triethylene glycol, an increase in the concentration of the cosolvent promotes the strengthening of the preparations and the growth of their thermal stability (incidentally, the addition of sucrose has the same effect on the properties of cryoPVAG [173]). Diethylene glycol occupies an intermediate position: for a content of the additive up to ~5%, weak cryogels are obtained, the cryogel being strengthened with increase in the concentration of diethylene glycol. It has been supposed that the strengthening effect of the OEG is caused by the liquid – liquid phase separation in the

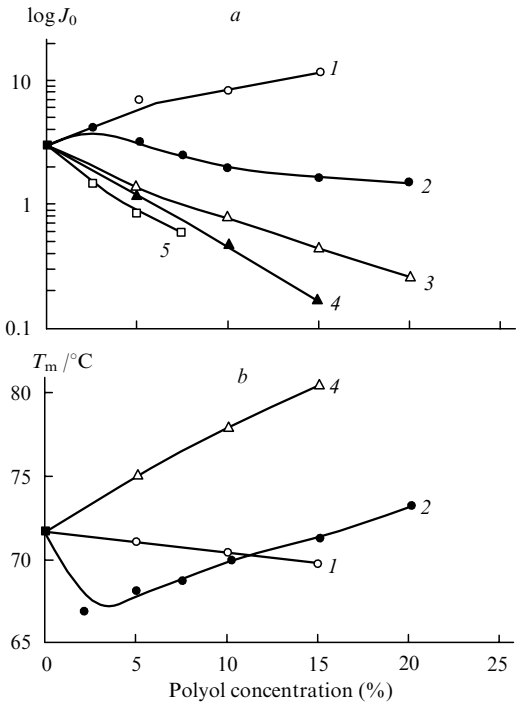


Figure 13. Rheological (*a*) and thermophysical (*b*) characteristics of cryogels formed at −20 °C (t_s = 24 h, v_{th} = 0.2 K min^{-1}) from 10% solutions of PVA (M = 81 700, DD = 98%) in the presence of added polyols of the ethylene glycol series: (*1*) ethylene glycol; (*2*) diethylene glycol; (*3*) triethylene glycol; (*4*) PEG-400; (*5*) PEG-1000.[172]

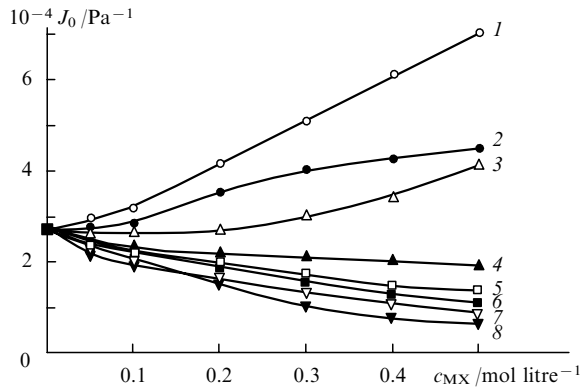


Figure 14. Rheological properties of cryogels formed at −20 °C (t_s = 24 h, v_{th} = 0.2 K min^{-1}) from 14% solutions of PVA (M = 69 000, DD = 98%) in the presence of low-molecular electrolytes MX at different concentrations[177] (*1*) NaSCN; (*2*) NaBr; (*3*) LiCl; (*4*) NaCl; (*5*) KCl; (*6*) NaOAc; (*7*) CsCl; (*8*) NaF.

unfrozen inclusions, whereas in the crystallisation of ice the system falls (on the phase diagram) into the region of thermodynamic incompatibility (liquid two-phase water – PVA – OEG systems are well known [174]) owing to the increase in the concentration of PVA and of the low-molecular polyol. As a result of this the gel forming agent is additionally concentrated in its 'own' (*i.e.* PVA-enriched) liquid microphase. On the other hand, an increase in the concentration of the polymer usually leads to the strengthening of the cryogel and to an increase in its melting point, which has been observed experimentally.

The influence of electrolytes on the cryotropic gelation of the polymer has been investigated.[54, 175–177] It was found that, in terms of the nature of their effect on the properties of the cryoPVAG formed from water – salt (MX) – PVA systems (Fig. 14), cations and anions can be arranged in a sequence corresponding to the positions of the corresponding ions in Hofmeister's lyotropic series, *i.e.* chaotropic ions (Li^+, Br^-, SCN^-, *etc.*), which destabilise hydrogen bonding, prevent to some extent the formation of strong cryoPVAG, whilst antichaotropic ions (Cs^+, F^-, OAc^-, *etc.*) promote the strengthening of the cryogels. Neutral electrolytes of the type of NaCl, which have a weak influence on hydrogen bonds, exhibit a small strengthening effect with increase in concentration as a consequence of phenomena involving the salting-out of the polymer.

Thus the composition of the solvent, *i.e.* its cryoscopic properties, the affinity for PVA, the effect of the medium components on hydrogen bonding, and also the salting-out and salting-in effects influence the cryotropic gelation of the polymer and hence the parameters of the cryogels obtained.

VI. Conclusion

By virtue of their high porosity and at the same time effective mechanical strength as well as stability in any biological media, the materials based on cryoPVAG have found extensive applications in various branches of biotechnology. Poly(vinyl alcohol) cryogels proved to be excellent carriers for the immobilisation of biological macromolecules [159, 178–187] and cells [4, 41, 188–265] and not only of microorganisms, which can stand quite well the cryogenic treatment, but also of certain animal cells.[266–268] Since the cryoPVAG are stable up to temperatures of 70–80 °C, the corresponding carriers have been used for the immobilisation of both mesophilic cells and thermophilic microorganisms,[210, 232, 237, 242, 245, 251] which functioned for more than a year at 60–65 °C without loss of activity.[242, 251] This is a record-breaking feature for biocatalytic systems entrapped in thermoreversible gel matrices. It has also been proposed that polyol cryoprotectors can be introduced for the simultaneous protection of cultures sensitive to freezing and in order to increase the strength characteristics of the gel carrier.[170, 172, 252]

Solid nutritional media have been developed on the basis of PVA cryogels for the culturing of microbial [269] and plant cells, in particular the ginseng biomass.[270] The use of such media makes it possible to replace the valuable nutrient gel former agar-agar by a synthetic polymer produced on a large scale. CryoPVAG coatings have found applications in the food industry for frozen fish and meat.[271–275] Chromatographic materials have been created from microgranulated cryoPVAG (0.2–0.3 mm),[276] while artificial bait for sporting and amateur fishing has been made from larger (2–3 mm) coloured granules or gel in the form of small fish-like objects.[13–17, 277] An interesting aspect of the employment of mixed cryogels (PVA + polyelectrolyte-type polymer) is the creation of mechanochemical actuators elements simulating the work of muscle (the studies in this field are being particularly vigorously prosecuted in Japan [127, 132, 278–292]). There have been scientific publications and a multiplicity of patents describing a wide variety of versions of polymer systems, employed in medicine, based on cryoPVAG (Refs 28, 29, 31–34, 90, 92, 93, 110, 120, 129, 131, 135, 137–143, 146–149, 154–161, 266, 268, 293–310) containing both PVA and its mixtures with other high-molecular-mass compounds and constituting composites with disperse fillers — inorganic (of the type of titanium dioxide) or organic (for example collagen fibres,[303, 310]) *etc.* These gels have been used successfully as substitutes for the cartilage tissue,[11] as protheses for surgery within the mouth,[11, 28, 29, 34, 148] as materials for ophthalmology [139] and dentistry,[147] as protective coatings for wounds and burns,[31, 135, 154] as cooling dressing, and cold helmets which do not secrete water for the prevention of hair loss in cancer chemotherapy,[31, 137, 138, 155–158, 293] and as special purpose catheters.[141]

The application of cryoPVAG as the gel medium for the tuning and calibration of NMR tomographs [120, 140, 143] and as systems for the controlled release of medicinal substances has been described.[12, 110, 129, 131, 142, 149, 161, 294, 297, 298, 302, 307, 309] Materials for cosmetics,[311, 312] *etc.* are being developed. Macroporous PVA membranes formed by cryogenic structure formation procedures may apparently find application.[123, 124, 153] The cryostructure formation process in PVA solutions has been proposed also for the preparation of artificial ice and snow [59, 313] and for the fixation of soils which have thawed out.[314]

There is no doubt that the successful application of the above materials in medicine and other branches of science and technology [145, 315–333] must be based on the fundamental knowledge of the mechanisms of the cryotropic gelation of PVA and of the influence of the polymer characteristics and also of the freezing–thawing parameters on the properties and structures of the cryogels formed under these conditions. All these factors promote their further comprehensive investigation. Studies on cryoPVAG are concerned with the mechanisms of gel formation,[334–336] the macroscopic properties of cryoPVAG and materials based on them,[337–343] and the structures of gels formed under different conditions,[344–347] on the one hand, and fine effects associated with the different states of the solvent molecules in such heterophase polymer systems,[348, 349] on the other. This is in fact the reason why attention has been concentrated in the review on these problems. The interested reader may become acquainted in detail with the practical applications of cryoPVAG in the literature quoted.

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