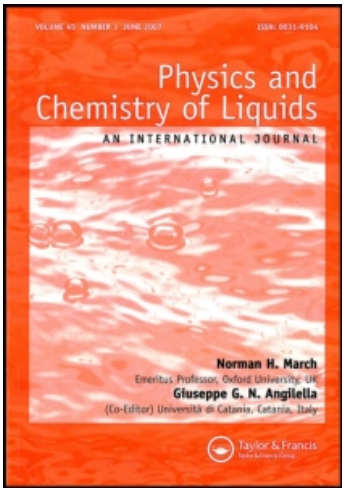

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Applications of activation energy and transition state theory for nucleos(t)ides and furanose helix puckering interactions in aqueous medium from 288.15 to 298.15 K

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Density $\rho/10^3\,\mathrm{kg\,m^{-3}}$, viscosity $\eta/10^{-1}\,\mathrm{kg\,m^{-1}\,s^{-1}}$ and surface tension $\gamma/\mathrm{N\,m^{-1}}$ of nucleosides (2-deoxy adenosine (DOA), thymidine (TMD)), nucleotides (guanosine monophosphate (GMP), adenosine triphosphate (ATP)) and their integral furanose sugar, 2-deoxy ribose (DOR) solutions have been measured at three different temperatures. The ρ values were used for apparent molal volume ($V_\phi/10^{-6}\,\mathrm{m^3\,mol^{-1}}$), η and γ calculations; η fitted in extended Jones–Dole equation for $B/\mathrm{kg\,mol^{-1}}$ and $D/(\mathrm{kg\,mol^{-1}})^2$ coefficients. The γ and V_ϕ were regressed against molality, m for limiting surface tension, γ^0 and apparent molal volume, $\overline{V}_2^0$ at $m \to 0$. Partial molal volume ($\overline{V}_1^0$) of water calculated from ρ values. Free energy of activation of viscous flow ($\Delta\mu_1^{0*}/\mathrm{kJ\,mol^{-1}}$) per mol of solvent was calculated from η_0 and $\overline{V}_1^0$ and $\Delta\mu_2^{0*}$ of solution from B and $\overline{V}_2^0$, and $\Delta\mu_2^{0*\mathrm{surf}}$ of dropwise flow of biomolecules from γ^0 and $\overline{V}_2^0$ values. The $\Delta\mu_2^{0*}$ and $\Delta\mu_2^{0*\mathrm{surf}}$ depict a state of activation energy for structure making and breaking of solvent. The B and γ^0 values are used to calculate transition state functions, $\Delta\mu_2^{0*} - \Delta\mu_1^{0*}$ and $\Delta\mu_2^{0*\mathrm{surf}} - \Delta\mu_1^{0*\mathrm{surf}} \geq 0$ or ≤ 0 for critical state molecular optimization to explain positive transitions of interacting heteromolecules. The V_2^0, $\Delta\mu_2^{0*}$ and $\Delta\mu_2^{0*\mathrm{surf}}$ are found to be negative inferring biomolecules as water structure breakers.

Keywords: Hydrophobicity; Apparent molal volume; Heteromolecular interactions and activation energy

1. Introduction

Since the last decade, activities of biomolecules/biopolymers in aqueous medium have been of biophysical interest [1,2]. As the state of energy and transitions play a key role in conformational changes, the concept that nucleosides, nucleotides and nucleic acid acting as not only cellular but also as extracellular signalling molecules, has drawn attention [3]. Such processes are associated with the system's spontaneity, and therefore theoretical and experimental efforts have become the thrust area

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of research [4] to evaluate the thermal and interaction volumes of heterocyclic bases and nucleosides described elsewhere [5,6]. Thermodynamic (V_ϕ), transport (η) and surface (γ) properties have been considered reliable and advantageous for interaction mechanism at cellular and intercellular matrix level [7]. Volumetric and viscometric studies of amino acids and proteins in hydrothermal solutions [8] along with enthalpies, heat capacities in *t*-butenol and compressibility have been studied by Yayanos [9] and Chalikian *et al*. [10]. Several types of interactions and free energy of some biochemicals in water [11] including transitions and electrostatic forces based on DLVO (Derjaguin–Landau–Verwey–Overbeek) density function theories [12] have been of some use. It is seen that physical properties of 2-deoxy adenosine (DOA), 2-deoxy ribose (DOR), guanosine monophosphate (GMP), adenosine triphosphate (ATP) and thymidine (TMD) as components of DNA and RNA have not been adequately studied yet except for the biological function [13]. Thus linkages, stabilization, genetic transformation and energy production in cell could be estimated for biotechnology and biophysics [14–16]. Our studies focus on hydration shell [17], van der Waals force [18], denaturation [19], hydrophobic effect [20], electrostriction of solvent [21] and conformational changes based on Frank and Frank model [22]. It facilitates an understanding of medical sciences [23–25] and energy storing mechanism in tissues and muscles [26]. Thus, molal volume illustrates the inter and intramolecular interactions of nucleos(t)ides to assess the nonionic backbone contribution to fully hydrated DNA and RNA molecules. It could demonstrate the effects of hydrophilic as well as hydrophobic interactions of $-CH_3$ and $-CH_2OH$ as side groups and structure making and breaking effects on water as postulated by Frank and Evans [27]. The transition state theory highlights the molecular energy states and is of potential biomedical significance to selectively stabilize and induce formation of higher order nucleic acid structures under physiological conditions. The partial molal volume rationalizes an amount of solute hydration and discriminates between the water molecules solvating the charged, polar, and nonpolar atomic groups of a solute. It has become a focal point of calculation of $\Delta\mu_2^{0*}$ function to resolve the interaction of biomolecules with water defined by transition state theory including dipole and van der Waals interactions, as opposed to solvent arrangement. However, less structured hydration around the bases were found to be local [28], and so biomolecules are referred to as 'water structure breaker' and intercalate themselves in water molecules. Thus the data of present studies could be considered as a readyreckoner for molecular modelling in any desired medium.

2. Experimental

DOA (Calbiochem, p. no. 2560), DOR (Serva feinbiochemica, Heidelberg, 18590), and ATP (A-2383), GMP (G-8377) and TMD (T-9250) were procured from Sigma, USA. Their purity was checked by HPLC and found to be of chromatographic grade. They were dried *in vacuo* for 48 h in P_2O_5 filled desiccator. Distilled and degassed water in nitrogen atmosphere and deionized by passing through Barnstead mixed bed ion-exchanger for solution w/w. Its conductivity was found to be $1 \times 10^{-7}\,\Omega^{-1}$. Density was measured with bicapillary (8 cm long with capillaries of 0.5 mm inner diameter) $25 \times 10^{-3}\,dm^3$ capacity pyknometer mounted on a stainless steel stand kept in the thermostat. The weight of solutions with pyknometer were measured with an electronic balance of 0.01 mg accuracy by Dhona model 100DS. The pyknometer was

calibrated with aqueous [29] NaCl and the viscometer with water at 298.15 K, the thermal stability of bath was better than ± 0.01 K, a Hewlett-Packard quartz thermometer calibrated with a gallium temperature standard measured the bath temperature. An accuracy of concentration of solutions was better than 1×10^{-5} mol kg^{-1}. Densities of water were taken from literature [27] and calibration was repeated immediately before and after each measurement, and the reproducibility was better than 1×10^{-5} kg m^{-3}. The flow time of solutions with low shear Ubbelohde viscometer [30] was noted with an electronic racer of 1×10^{-2} s.

3. Results

The ρ values were calculated from weights using buoyancy correction $0.0012(1-(W/W_0))$ for air, W and W_0 are weights of solution- and solvent-filled pyknometer. Error in ρ values were calculated from weights with the reproducibility to one part to 1×10^{-5} mol kg^{-1} [30]. The V_ϕ^0 values were calculated as in equation,

$$V_\phi^0 = \left[\frac{1000(\rho_0 - \rho)}{m\rho\rho_0}\right] + \left(\frac{M}{\rho}\right). \tag{1}$$

The M, molal mass of biomolecules, error in V_ϕ^0 were calculated from $V_\phi^0 = \pm\Delta\rho \times 1000\,\mathrm{m}^{-1}$ relation, ρ data was fitted to polynomial relation with m as

$$\rho = \rho^0 + S_d m + S_d' m^2 \tag{2}$$

and V_ϕ^0 data were fitted to Masson's [31] equation

$$V_\phi = V_\phi^0 + S_v m^{1/2} + S_v' m. \tag{3}$$

As usual, ρ^0 and V_ϕ^0 are limiting values and, S_d and S_v slope constants given in tables 1 and 2, η data were analysed with Jones–Dole equation [32]

$$\eta_r = \frac{\eta}{\eta_0} = 1 + Am^{1/2} + Bm. \tag{4}$$

Here A is Falkenhagen coefficient to measure the molecular interactions and B, the Jones–Dole coefficient. Coefficient A is applicable for electrolytes, so an extended Jones–Dole equation is used for our systems as

$$\eta_r = \frac{\eta}{\eta_0} = 1 + Bm + Dm^2. \tag{5}$$

On the lines of Feakins *et al.*, [37] the B values are fitted to transition state theory for $(\Delta\mu_2^{0*} - \Delta\mu_1^{0*})$ determination as

$$B = \left(\frac{V_1^0 - V_2^0}{1000}\right) - V_1^0\left[\frac{(\Delta\mu_2^{0*} - \Delta\mu_1^{0*})/RT}{1000}\right]. \tag{6}$$

Table 1. Densities ($\rho \pm 1 \times 10^{-5}$ kg m^{-3}) and apparent molal volume (V_ϕ, 10^{-6} m^3 mol^{-1}) of aqueous sodium chloride systems.

	Aqueous NaCl at 298.15			
m (mol kg^{-1})	ρ (10^3 kg m^{-3}) (Exp.)	ρ (10^3 kg m^{-3}) (Lit.)	V_ϕ (10^{-6} m^3 mol^{-1}) (Exp.)	V_ϕ (10^{-6} m^3 mol^{-1}) (Lit.)
0.05	0.99968		17.11	
0.10	1.00163	1.00116	17.20	17.06
0.25	1.00748		17.46	
0.50	1.01723	1.01711	17.90	17.87
0.75	1.02698		18.33	
1.00	1.03673	1.03630	18.77	18.41
1.25	1.04648		19.21	

Lit, Reference [29].

Table 2. Limiting density (ρ_0) and apparent molal volumes (V_ϕ^0) and their slope constants S_d, and S_v and S_v' obtained on regression of primary data against temperature T/K. The values written after ± represent error in the respective functions.

T/K	$\rho_0 \pm 2 \times 10^{-5}$ (10^3 kg m^{-3})	$S_d \pm 2 \times 10^{-7}$ (10^3 kg^2 m^{-3} mol^{-1})	V_ϕ^0 (10^{-6} m^3 mol^{-1})	$S_v \pm$ x 10^5 (10^{-6} kg m^3 mol^{-1})	$S_v' \pm 10^8$ (10^{-6} kg^2 m^3 mol^{-3})
			2-Deoxy adenosine		
288.15	0.99933	1.0152 ± 5	−1839.18 ± 103.24	15.24 ± 129954	−6.28 ± 5
293.15	0.99917	0.1630 ± 80	−3935.18 ± 103.21	50.15 ± 129913	−18.94 ± 5
298.15	0.99817	0.1848 ± 90	−4698.15 ± 103.17	60.16 ± 129867	−22.97 ± 5
			2-Deoxy ribose		
288.15	0.99973	0.0523 ± 30	−2666.81 ± 103.24	35.32 ± 129953	−13.71 ± 5
293.15	1.00057	−3.1178 ± 0.02	−6916.56 ± 103.21	11.53 ± 129910	−50.11 ± 5
298.15	0.99811	−0.0794 ± 40	−4411.37 ± 103.71	59.54 ± 129867	−23.15 ± 5
			Guanosine monophosphate		
288.15	0.99977	1.0204 ± 5	−3284.58 ± 103.24	31.52 ± 129953	−11.40 ± 5
293.15	0.99882	0.3892 ± 2	−2783.78 ± 103.21	37.40 ± 12914	−14.95 ± 5
298.15	0.99798	0.1857 ± 90	−3752.19 ± 103.17	50.20 ± 129868	−19.23 ± 5
			Adenosine triphosphate		
288.15	0.99977	0.3728 ± 2	−3124.87 ± 103.24	46.74 ± 129952	−19.42 ± 5
293.15	0.99893	0.3687 ± 2	−2492.59 ± 103.21	29.43 ± 129914	−9.96 ± 5
298.15	0.99819	0.1196 ± 60	−4531.96 ± 103.17	−0.05 ± 129867	−24.65 ± 5
			Thymidine		
288.15	0.99979	0.1515 ± 80	−2933.56 ± 103.24	38.98 ± 129953	−15.17 ± 5
293.15	0.99894	0.1813 ± 90	−3430.46 ± 103.21	48.38 ± 129913	−19.82 ± 5
298.15	0.99787	0.0318 ± 20	−3247.41 ± 103.17	43.13 ± 129868	−16.36 ± 5

$\overline{V}_1^0$, $\overline{V}_2^0$ and $\Delta\mu_2^{0*}$ are contributions per mole of solute to free energy of activation of viscous flow. Thus, $\Delta\mu_1^{0*}$ and $\Delta\mu_1^{0*\text{surf}}$ were calculated from

$$\Delta\mu_1^{0*} = RT\ln\left(\frac{\eta_0\overline{V}_1^0}{hN}\right) \tag{7}$$

$$\Delta\mu_1^{0*\text{surf}} = RT\ln\left(\frac{\gamma^0\overline{V}_1^0}{hN}\right). \tag{8}$$

If R is Rydberg constant, h is Planck constant, N is Avogadro's number, then $\Delta\mu_2^{0*}$ and $\Delta\mu_2^{0*\text{surf}}$ are obtained from

$$\Delta\mu_2^{0*} = \Delta\mu_1^{0*} - \left(\frac{RT}{\overline{V}_1^0}\right)\left(1000B - \left(\overline{V}_1^0 - \overline{V}_2^0\right)\right) \tag{9}$$

$$\Delta\mu_2^{0*\text{surf}} = \Delta\mu_1^{0*} - \left(\frac{RT}{\overline{V}_1^0}\right)\left(1000\gamma^0 - \left(\overline{V}_1^0 - \overline{V}_2^0\right)\right) \tag{10}$$

The $\Delta\mu_2^{0*}$ has positive and larger values than $\Delta\mu_1^{0*}$, predicting the viscous flow as a difficult process with a complex of biomolecules due to interaction with water.

4. Discussion

4.1. *Densities*

The ρ for 0.050 to 1.25 mol kg^{-1} aqueous NaCl was measured to determine V_ϕ^0 values, and the reproducibility was found to be $\pm 0.05 \times 10^{-6}$ m^3 mol^{-1}, having close agreement with literature [29]. It authenticates our experimental procedure (table 1). Densities are found to be higher than water by about 0.00975×10^{-3} kg m^{-3} at each temperature (table 2), indicating an assertion of internal pressure on water with structure breaking, which enhances with concentrations due to stronger intermolecular forces. The decrease in ρ values for 293.15 K is more, thus concentration strengthens the homomolecular interactions due to temperature, with much reorientation in the forces. Likewise, higher ρ values for DOR than for other systems, is to be rationalized for effective structure breaking action of adenine due to free –NH_2 and four –N atoms with free deoxy ribose. Therefore, the composition of DOA favours biomolecular interactions through hydrogen bonding, although, ρ values for DOR, GMP and ATP are noted to be lower than that of TMD due to weaker intermolecular forces. However, densities of DOA, DOR, GMP, ATP and TMD are higher than water by about 0.00875×10^{-3} kg m^{-3} at each K, which infer stronger intermolecular forces of same order with slightly higher forces for DOR. A decrease in ρ of 0.00134×10^{-3} kg m^{-3} per 5 K is found lower than water, denies withstanding of interaction due to water unlike water–water with structure breaking effect of nucleos(t)ides. An increase in ρ values by 0.00023×10^{-3} kg m^{-3} for TMD against water implies a water–DOR interaction complex more compact than the other systems. A density at 298.15 for DOR and TMD is noted to be higher by 0.00045×10^{-3} kg m^{-3} than that of 288.15 K. These compounds are assumed to exhibit stronger binding forces for DNA and RNA strands. A 0.00089×10^{-3} kg m^{-3} decrease in the density for water from 288.15 to 293.15 K against a 0.00016×10^{-3} kg m^{-3} for DOA concludes a larger structure breaking effect of temperature on water than on DOA. The trend remains the same for DOA, DOR, GMP, ATP and TMD due to the presence of stronger intermolecular forces than of water itself, inferring higher resistance to thermal forces of such biomolecules than to water. The interactions can be correlated to their geometry where, water dipoles interact with the polar centres of biomolecules while DOR has a mild effect on hydrogen bonding of water and a slightly stronger effect on nucleosides and nucleotides.

The order of density at 288.15 K, TMD > GMP = ATP > DOR > DOA illustrates stronger interactions of TMD than other temperatures. Two oxygen atoms of pyrimidine ring attached to a ribose sugar of TMD cause stronger hydrophilic interactions, and the PO_4^{3-} groups of GMP and ATP induce a weakening of the forces. Thus, V_ϕ^0 decreases by 1800 for DOA, 500 for DOR, $300 \times 10^{-6}\,m^3\,mol^{-1}$ for TMD at each K enforcing of PO_4^{3-} with its number with slightly stronger intermolecular forces. Three PO_4^{3-} groups along with the sugar pucker and the purine ring have been used to produce slightly higher densities 'as more the phosphate groups in the nucleotides stronger are the intermolecular forces'. The values for DOR are higher than DOA [33] by $0.00003 \times 10^{-3}\,kg\,m^{-3}$ at 288.15 and at 293.15 K in the order DOR > DOA > ATP > GMP > TMD with 0.001, 0.00002 and $0.00011 \times 10^{-3}\,kg\,m^{-3}$ respectively. So, temperature effectively destabilizes the molecular forces of TMD with stronger forces of DOR sugar, with water favouring the generation of forces due to H atoms and –OH groups with an ATP > DOA > DOR > GMP > TMD order of density at 298.15 K, and with 0.00002, 0.00006, 0.00006 and $0.00013 \times 10^{-3}\,kg\,m^{-3}$ at 298.15 K respectively, higher values for ATP at 298.15 than at 288.15 K and 293.15 K, and the same ρ values for TMD as of 293.15 K, inferring higher intermolecular forces at 298.15 than at 293.15 K. It could reveal that thermal energy excites electrons causing electronic, translational and orientation transitions, setting right the molecule in an optimum position with higher ρ at higher K.

The GMP > DOA > ATP > TMD > DOR, GMP > ATP > TMD > DOA > DOR and GMP > DOA > ATP > TMD > DOR order of S_d values at 288.15, 293.15 and 298.15 K respectively, reflects a higher concentration influence of GMP on pairwise interactions. It illustrates that a single phosphate group being the active centre for interactions along with oxygen atom in purine ring, –N atom with lone pair of electrons and –OH in sugar helix of GMP cause additional intermolecular forces and are responsible for GMP–GMP interactions. Contrary to this, DOR S_d values are lowest at each Kelvin and denote its significant role in pairwise interactions. The order of the remaining biomolecules shows a preferential strength of influence of composition on homomolecular interactions. However, at 288.15 and 298.15 K, the forces generated by the biomolecules remain of same strength but at 293.15 K, ATP becomes more active (table 2).

4.2. *Apparent molal volume*

Also, DOA > TMD > DOR > ATP > GMP order of V_ϕ^0 at 288.15, reverse of ρ^0, supports slightly weaker interactions of DOA than 293.15 and 298.15 K, predicting stronger intermolecular forces for lower V_ϕ^0 (table 2). The negative V_ϕ^0 values have been obtained proclaiming exceptionally stronger heteromolecular interactions. A $1000(\rho_0 - \rho)/m\rho\rho_0$ term decides a magnitude of V_ϕ^0, if $1000/m$ remains constant for an individual composition even though $(\rho_0 - \rho)/\rho_0$ should be fixed. The stronger solute–solvent interactions produce higher ρ than ρ_0, so $1000(\rho_0 - \rho)/m\rho\rho_0$ gives positive values (equation (1)). The molecular masses of compounds are between 269.1 to 551.1 $g\,mol^{-1}$ thus on dividing by ρ, gives lower values than these obtained on solving $1000(\rho_0 - \rho)/m\rho\rho_0$ term. Hence, negative V_ϕ^0 values significantly describe the intermolecular forces operating between the nucleotides and nucleosides, and water. So an actual shrinkage [34] in V_ϕ^0 occurs on attraction for water with a stronger compaction than their own volume and negative V_ϕ^0 serves to emphasize that an excess

Table 3. Limiting viscosity (η_0) and slope constant (S_η) obtained by least square fit of η data against molality. The η, $kg\,m^{-1}\,s^{-1} = 10^3\,g \times 10^{-2}\,cm\,s^{-1} = 10\,g\,cm^{-1}\,s^{-1}$. The values written after $\pm$ represent error in the respective functions.

T/K	$\eta_0 \pm 1 \times 10^{-4}$ ($10^{-3}\,kg\,m^{-1}\,s^{-1}$)	$S_\eta \pm 10^{-8}$ ($10^4\,kg\,m^{-1}\,s^{-1}\,mol^{-1}$)
	2-Deoxy adenosine	
288.15	1.1090	3.2964 ± 20
293.15	1.0031	11.9420 ± 2
298.15	0.8906	6.2891 ± 2
	2-Deoxyribose	
288.15	1.1125	-1.5827 ± 2
293.15	1.0164	-13.0850 ± 3
298.15	0.9762	6.9440 ± 3
	Guanosine monophosphate	
288.15	1.1111	-4.5296 ± 1
293.15	1.0237	-37.1600 ± 8
298.15	0.9826	-9.8927 ± 3
	Adenosine triphosphate	
288.15	1.1028	5.2824 ± 70
293.15	1.0122	-19.2550 ± 4
298.15	0.9064	-13.5130 ± 4
	Thymidine	
288.15	1.1175	-8.7248 ± 1
293.15	0.9859	20.8900 ± 4
298.15	0.8908	3.3119 ± 1

and partial molal volume are coefficients. Like density, V_ϕ^0 and B (tables 2 and 3) depict similar trends and are static, and the transport, properties respectively illustrate an exceptional behaviour of phosphate viz. ATP and GMP with temperature. It concludes a crucial role of thermal energy for phosphate–water interactions, as phosphate groups introduce an element of asymmetry in molecules pushing to a most stable optimization. As per the flickering model, water molecules surround and adhere to the phosphates for a stable conformation to have V_ϕ^0 values (table 4), which usefully support the trend of each other with temperatures. Thus DOA and DOR without phosphate groups have almost similar V_ϕ^0 values with prominent hydrophilic interactions as ribose contains only sugar part but DOA contains purine base + sugar unit with nitrogen atoms and amino group in the purine ring. Pyrimidine rings of TMD with electron deficient methyl ($-CH_3$) group causes hydrophobic interactions with some deviations.

4.3. *Viscosities*

The η^0 at 288.15 K is found to be lower by $1.2\,kg\,m^{-1}\,s^{-1}$, at 293.15 and 298.15 K higher by $3.9\,kg\,m^{-1}s^{-1}$ than water. TMD > DOR > GMP > DOA > ATP at 288.15, GMP > DOR > ATP > DOA > TMD at 293.15 and GMP > DOR > ATP > TMD > DOA at 298.15 K order of η^0 infer stronger Newtonian forces for TMD and GMP. At 288.15 K, the η^0 values are found to be lower than water by 22.9 to $37.6\,kg\,m^{-1}\,s^{-1}$, raising the temperature by 5 K; η^0 is found to be higher than water by 5.2 to $21.1\,kg\,m^{-1}\,s^{-1}$ (tables 2 and 3) close to the values of 298.15 K. It demarcates slightly stronger water structure breaking effect with temperature. Differences in η^0 values are 5.0, 1.4, 2.1 and $6.2\,kg\,m^{-1}\,s^{-1}$ at 288.15 K; 37.8, 4.2, 9.1 and $17.2\,kg\,m^{-1}\,s^{-1}$ 293.15 K; 6.4, 69.8, 15.6 and $0.2\,kg\,m^{-1}\,s^{-1}$ at 298.15 K respectively and apparently

support the water structure breaking nature of species. The η^0 of water is higher than systems at each temperature forecasting a weaker effect of Newtonian forces on the water–biomolecule interactions with destabilization in long range arrangement of water structure. Although η^0 of water at 288.15 K is higher but at 293.15 and 298.15 K lower than that of systems (table 4), as the structure is broken, water molecules resist free flow causing torsional forces to interact with uniform forces in viscous flow. Density, a static property, illustrates electrostatic forces, so torsional forces remain defunct and several water molecules surround biomolecules forming a orderedness in the structured geometry behaving like a laminar or Newtonian flow in micro capillary. Molecules which move along with each other as per cage model of water, so that η^0 results prove the biomolecules to be water structure breakers with lower values. Trends of V_ϕ^0 and ρ are resolved considering Newtonian flow for water and solutions resulting in lesser density of water than the solution. Also, a change in the dipole moment compensates for changes, as centripetal forces of water are functional causing compactness reducing the volume. It is rationalized with dipolar interactions breaking the water structure due to partially charged centres with a higher magnitude than water. Water monomers become the hub for water-nucleosides and nucleotides and have stronger structural interactions.

4.4. *Surface forces*

The γ^0 values for biomolecules are found to be higher than water by $2.223 \times 10^{-2}\,\mathrm{N\,m^{-1}}$ at each temperature. Stronger surface forces than that of water are noted due to stronger hydration spheres around such molecules. The order of values is listed as TMD > GMP > ATP > DOR > DOA, ATP > DOR > TMD > GMP > DOA and TMD > ATP > GMP > DOA > DOR at each K respectively. It differs from the orders of the V_2^0 and η_2^0 values, and proves that γ_2^0 elucidate the state of cohesive and adhesive forces rather than electrostatic and Newtonian forces. Generally γ_2^0 decreases with temperature but DOR and ATP from 288.15 to 293.15 K increase by 5.113 and $7.823\,\mathrm{N\,m^{-1}}$. It decreases by 4.690 and $10.948 \times 10^{-2}\,\mathrm{N\,m^{-1}}$ from 293.15 to 298.15 K with maximum γ_2^0 values for TMD at 298.15 K. The values prove that DOR and ATP reorient water structure and become more accessible at 293.15 K, attributed to the surface forces due to large number of H^+ and OH^- ions. Likewise, ATP due to PO_4^{3-} favours the generation of forces in a similar manner, but for purine and helix sugar units with larger number of hydrogen and oxygen atoms, the thermal energy favours generation of stronger forces. This infers that DNA and RNA bear with the temperature and destabilize at 288.15 K, the larger γ_2^0 values of TMD imply stronger intermolecular forces. Thus these two units are structure strengthening although DOR with DOA seem less effective in this regard, but at 293.15 K DOR seems to cause stronger surface forces and DOA, GMP and TMD cause weaker surface forces by 2.874, 2.597 and $2.491 \times 10^{-2}\,\mathrm{N\,m^{-1}}$ respectively from the previous temperature. Exceptionally higher values for ATP show larger activity at 293.15 K rather than the previous and later temperatures. At 298.15 K, these molecules except for TMD produce considerably lower values but at 288.15 K, the TMD shows greater cohesive and adhesive forces than other biomolecules except ATP and TMD at 293.15 and 298.15 K respectively. It can be concluded that phosphate backbone in compounds do cause stronger adhesive and cohesiveness, inhibiting a free flow. Thermodynamic (ρ and V_2^0 with electrostatic) and transport

(η^0 and B with continuous-Newtonian and γ_2^0 with broken-adhesive and cohesive forces) have been visualized in isolation as complementary to each other. An activation energy function derived by a combination of any two parameters has been calculated (equations (9) and (10)), termed as $\Delta\mu_2^{0*}$ (from Newtonian flow) and $\Delta\mu_2^{0*\text{surf}}$ (dropwise flow).

The $\Delta\mu_2^{0*}$ and $\Delta\mu_2^{0*\text{surf}}$ are found to be in the order of DOR > GMP > DOA > ATP > TMD, DOA > GMP > ATP > DOR > TMD and DOA > DOR > ATP > GMP > TMD at 288.15, 293.15 and 298.15 K respectively. Again ATP with larger number of $-PO_4^{3-}$ groups needs higher activation energy for viscous flow at lower temperature and DOA at higher temperature. TMD requires lower $\Delta\mu_2^{0*}$ at each temperature (figure 1). It is clear that higher energy from the system for nucleoside ring with $3(-PO_4^{3-})$ groups is due to its asymmetry in structure. While DOA without $-PO_4^{3-}$ groups show higher $\Delta\mu_2^{0*}$ values at 293.15 and 298.15 K respectively,

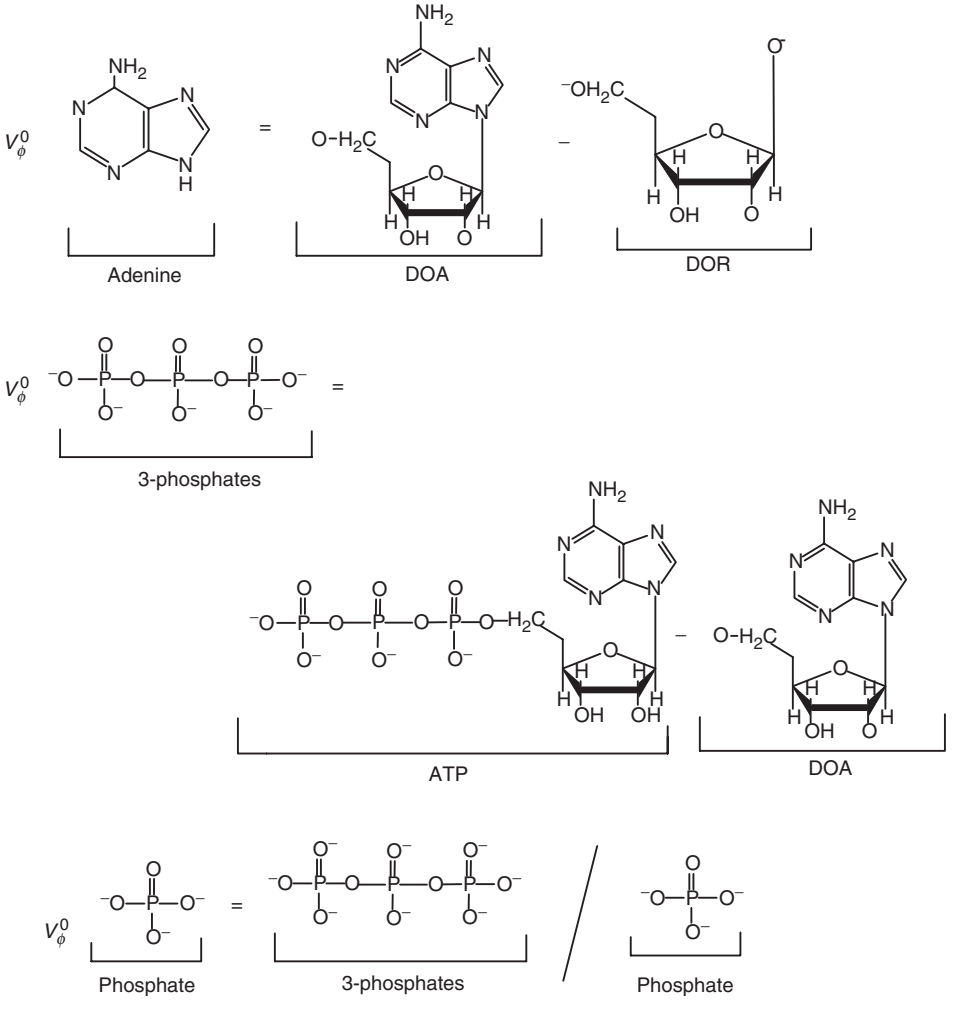

Figure 1. The structures of the nucleoside and nucleotide and their subunits for evaluation of limiting apparent molal volumes as in table 5.

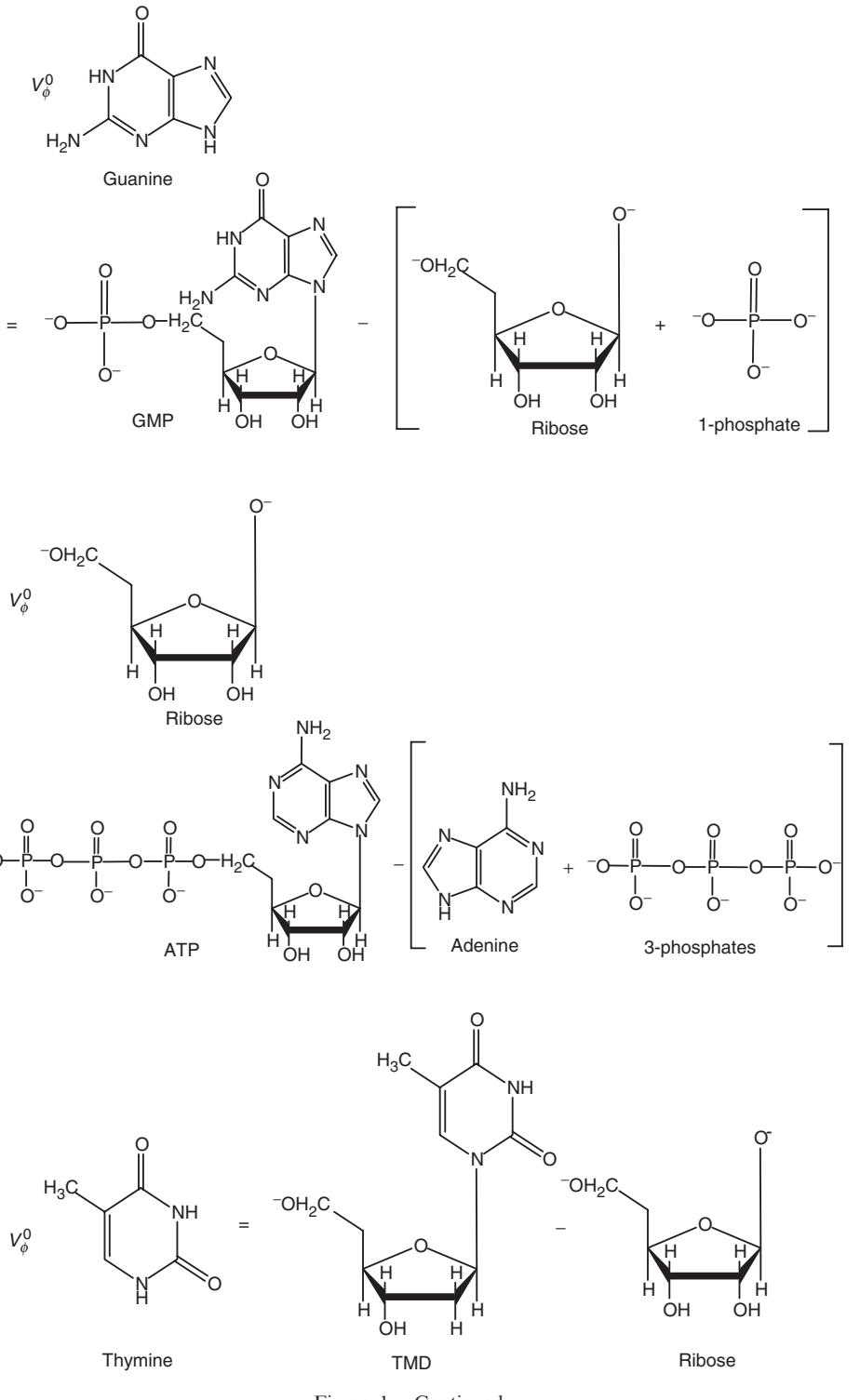

Figure 1. Continued.

Table 4. The $\rho_0(T)$, $V_\phi^0(T)$, $\eta_0(T)$ and $B(T)$ functions when $T \to 0$ of the aqueous solution systems.

Systems	ρ_0 (10^3 kg m^{-3})	$V_\phi^0(T)$ (10^{-6} m^3 mol^{-1})	η_0 (10^{-3} kg m^{-1} s^{-1})
2-Deoxy adenosine	1.03290	2.00	7.4033
2-Deoxy ribose	1.04696	10.00	5.0307
Guanosine monophosphate	1.05133	3.00	4.8061
Adenosine triphosphate	1.05388	−5.00	6.7646
Thymidine	1.05515	1.00	7.6438

Table 5. The molal volume contribution of adenine, guanine, thymine, guanosine and phosphates.

Simulations of V_ϕ^0 of molecules Systems	V_ϕ^0 (10^{-6} m^3 mol^{-1}) (T/K)		
	288.15 K	293.15 K	298.15 K
V_ϕ^0 Adenine = V_ϕ^0(2-Deoxy adenosine − 2-Deoxy ribose)	827.67	2981.38	−286.78
V_ϕ^0 3P = V_ϕ^0 (Adenosine triphosphate − 2-Deoxy adenosine)	−1285.69	1442.59	166.19
V_ϕ^0 1P = V_ϕ^0 (3Phosphate/3)	−428.56	480.86	55.39
V_ϕ^0 Guanine = V_ϕ^0(Guanosine monophosphate – (ribose + 1 phosphate))	−189.17	2690.19	492.99
V_ϕ^0 Ribose = V_ϕ^0(Adenosine triphosphate − (adenine + 3 phosphate))	−2666.85	−5954.83	−4411.37
V_ϕ^0 Thymine = V_ϕ^0(Thymidine − Ribose)	−266.71	2524.37	1163.96
V_ϕ^0 Guanosine = V_ϕ^0(Guanosine monophosphate − 1 phosphate)	−2856.02	−3264.64	−8163.56

probably adenine base and sugar pucker involve in stronger hydrophobic and hydrophilic interactions respectively, so their hydrodynamic volume needs more activation energy for the viscous flow; and individually decrease with temperature, thus $(\Delta\mu_2^{0*} - \Delta\mu_1^{0*})$ values are noted as DOA < DOR < TMD < ATP < GMP, ATP < GMP < TMD < DOA < DOR and TMD < GMP < DOR < ATP < DOA at 288.15, 293.15 and 298.15 K respectively. The $(\Delta\mu_2^{0*} - \Delta\mu_1^{0*}) > 0$ infers structure maker and $(\Delta\mu_2^{0*} - \Delta\mu_1^{0*}) < 0$ breaker, interestingly $(\Delta\mu_2^{0*\text{surf}} - \Delta\mu_1^{0*\text{surf}})$ orders resemble the magnitude of latter values. Thus an order of $\Delta\mu_2^{0*}$ reinforces our earlier contention derived from V_2^0, B and γ_2^0 that strong solute–solvent interactions exist. The $\Delta\mu_2^{0*}$ is acquired from solutes itself facilitating interactions and its redistribution occurs to form intermolecular nonreacting bonds (table 6). $\Delta\mu_1^{0*}$ values are positive for water predicting formation of weaker transition state. Thus $\Delta\mu_2^{0*}$ negative values for GMP, DOR and TMD predict the formation of a stronger transition state responsible for breaking and making a distortion of heteromolecular bonds. The $\Delta\mu_2^{0*}$ positive values at 288.15 K illustrate stronger water structure breaker with weak formation of transition state as compared to a higher temperature, its values at 293.15 and 298.15 K infer destabilization of water structure a facilitating factor for biomolecules behaving as water structure maker. Although at higher temperature the molecules behave as breaker due to thermally destabilized water that do not require much $\Delta\mu_2^{0*}$ for transition state and develop the hydration shell with a combination of less $\Delta\mu_2^{0*}$. Our results resemble an order noted by Feakins *et al.* and Kannapan, however the dielectric constant of water caused by the biomolecules may play a key role to monitor the interactions, for binary systems with $\Delta\mu_2^{0*} - \Delta\mu_1^{0*} < 0$. These values prove structure breaking as compared to higher values at 288.15 K, thus the process of viscous flow becomes difficult with concentrations. In this context, the solutes cause much hindrance in the viscous flow due to their sensitiveness

Table 6. Free energy of activation of viscous ($\Delta\mu_2^{0*}$) and dropwise flows ($\Delta\mu_2^{0*surf}$) for nucleosides, nucleotides and 2-deoxyribose sugar at three temperatures. The $\Delta\mu_2^{0*surf}$ from γ^0, the coefficient of surface tension. The 18.00, 18.03 and $18.05 \times 10^{-6}\,m^3\,mol^{-1}$ are V_1^0 values for water at 288.15, 293.15 and 298.15 K.

Systems	γ^0	V_2^0	$\Delta\mu_2^{0*}$	$\Delta\mu_2^{0*surf}$	$\Delta\mu_2^{0*} - \Delta\mu_1^{0*}$	$\Delta\mu_2^{0*surf} - \Delta\mu_1^{0*surf}$
			288.15 K			
DOA	75.713	−1839.18	17374.165	−9780.724	−264.217	−237.062
DOR	75.803	−2666.81	29487.312	−9682.567	−386.354	−347.184
GMP	77.684	−3284.58	18772.130	−9850.666	−457.764	−429.141
ATP	77.305	−3124.87	15398.816	−9821.485	−433.159	−407.939
TMD	78.687	−2933.56	10383.059	−10030.847	−402.711	−382.297
			293.15 K			
DOA	72.849	−3935.18	2103.076	−9263.950	−535.846	−524.479
DOR	80.717	−6916.56	−939.379	−9924.438	−935.372	−926.386
GMP	74.087	−2783.78	−9704.093	−9586.907	−368.569	−368.686
ATP	81.995	−2492.59	4994.661	−10695.13	−343.949	−328.259
TMD	76.196	−3430.46	−6752.324	−9784.558	−458.840	−455.808
			298.15 K			
DOA	69.067	−4698.15	2192.673	−8786.877	−649.068	−638.088
DOR	68.993	−4411.37	−57248.290	−8816.093	−550.289	−598.721
GMP	70.957	−3752.19	−55395.890	−9176.277	−461.721	−507.941
ATP	71.047	−4531.96	−10191.560	−9081.566	−613.887	−614.997
TMD	82.700	−3247.41	1094.465	−10857.993	−448.971	−437.018

Units: $B/kg\,mol^{-1}$, $\gamma^0/10^{-2}\,N\,m^{-1}$, $V_2^0/10^{-6}\,m^3\,mol^{-1}$, $\Delta\mu_2^{0*}/kJ\,mol^{-1}$.

for temperature or due to the complex structural configuration with respect to polar groups of biomolecules. The difference between $\Delta\mu_2^{0*}$, $\Delta\mu_2^{0*surf}$ is 26.938, 39.17, 27.859, 25.22, 20.414 kJ mol^{-1} for DOA, DOR, GMP, ATP and TMD respectively at 288.15 K. At 293.15 it is 11.367, 8.986, −0.117, 15.69 and 3.032 kJ mol^{-1}, and 10.98, −48.432, −46.22, −1.11 and 11.953 kJ mol^{-1} respectively at 298.15 K. Thus, it can be explained that the Newtonian and Brownian motion affect the required activation energy for molecules. For $\Delta\mu_2^{0*surf}$, these forces do not work so the values are approximately higher than $\Delta\mu_2^{0*}$. It appears that at higher temperatures, ATP and GMP show a little discrepancy in behaviour due to relative planar stacking of the aromatic base along with helix sugar pucker and PO_4^{3-} backbone have some additional forces for the molecules.

As cyclodextrins with an inner cavity is reported to be hydrophobic [35,36], thus DOR resembles a behaviour having hydrophilic outer surface and hydrophobic inner cavity. So partly favouring key–lock interactions and determined by hydrophilic interactions due to oxygen atom in the furanose sugar, DOR, seems to create some hydrophilic environment at the outer surface. It is also expected from the data that the hydrophilic interactions with approximately the same magnitude would dominate over the hydrophobic interactions. These interactions are important for nucleos(t)ides of nucleic acids do cause hydrogen bonding between them and charge repulsion at a negatively charged phosphoribose backbone.

5. Biological significance

Thermodynamic and transport profiles of biopolymers have been pivotal tools for modelling and energy optimization of molecules. Thus density and apparent

molal volume of molecules being constituted by spatial interacting electronic motions promulgate cohesive and adhesive forces. Such models of biomolecules with definite magnitude of residual forces lead to determine Brownian and Newtonian motions along with electrostatic forces responsible for friction forces owing to the flow dynamics of solutions. Thus, our studies render substantial help for a primary characterization solvents along with their structural reorientation. As DOA, DOR, GMP, ATP and TMD are constituents of DNA and RNA, and energy sources in biological systems, thus a better understanding about role of genetic materials and energy releasing processes could be illustrated with the state activation energy. The ρ, V_ϕ^0 and η^0 are intensive and define intermolecular interactions of monomer and biopolymers as well. The studies are of bioengineering significance and lead to the establishment of biothermodynamics. Customarily, blood is a transporting fluid in a fixed inner diameter of capillaries. Thus larger sized hydrodynamic units of such biomolecules may hinder the flow of blood and the transport of other biomolecules.

6. Conclusion

Density, volume and viscosity of biomolecules are of fundamental interest for structural modifications in solutions, especially the structure breaking effect on water along with their Newtonian behaviour on flow. The trends of V_ϕ^0 values with temperature signify the role of thermal energy to reorient the forces. Especially at 293.15 K, the ATP develops the weakest forces and thymidine is stronger, but at 288.15 K, the thymidine forces are weaker. Here, ribose unit seems to be sandwiched and a center of hydrophilic interactions.

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