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# Adsorption of Nucleotides on Clay Surfaces. Effects of mineral composition, pH and solution salts.

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## Abstract:

In the context of the origin of life, the adsorption of nucleotides onto clay surfaces has been tackled through classical molecular dynamics calculations. The effect of the mineral composition, pH and solution salts has been explored. It was firstly observed that cation adopts a layered structure above mineral surfaces which changes as a function of mineral composition and surface charge location, and has substantial effects on nucleotide adsorption. If the mineral charge is located in the octahedral (inner) layer of montmorillonite, the first two layers are less populated while the third comprises the majority of cations. For nontronite, which presents negative charges in the tetrahedral layer in contact with solutes, the first two layers concentrate the majority of cations. The negative charge on clay surface is thus screened by the first two layers for nontronite, and the third layer for montmorillonite. As a result, negatively charged phosphate moiety of nucleotides, which coordinates cations, can approach closer to the surface and the nucleobase binds better to the surface of nontronite compared to montmorillonite. As such, the nucleobase interacts in a parallel configuration stabilized by Van der Waals interactions with the surface. This observation explains the experimental results on the effect of mineral composition as well as pH and aqueous cations. Indeed, at pH=3, the nucleobase and phosphate protonation states lead to a different adsorption mode, where phosphate does not play any role whilst the positively charged nucleobase does participate actively in binding to the clay surface through electrostatic interactions. In presence of divalent cations in solution, the phosphate does coordinate exclusively to the divalent cations. Ca<sup>2+</sup> cation exchange in the second layer allows the coordinated phosphate to approach closer to the surface and leads to nucleobase adsorption in a parallel configuration.

### 33 **Introduction.**

34 In the prebiotic context that requires to form complex biomolecules, the role of clay minerals is still a  
35 matter of debate. As a result of aqueous or hydrothermal alteration of the seafloor iron magnesium  
36 rich silicates, clay minerals were already abundant on Earth during late Hadean or early Archean  
37 periods when life originated (Hazen et al., 2013; Pearce et al., 2018). These clays have been recognized  
38 to offer multiple interesting properties for the potential concentration and polymerization of the  
39 building blocks of biomolecules present in the first living organisms. The primitive seawater was  
40 probably very dilute in organics (Miller, 1987), primitive atmosphere had no ozone layer, therefore  
41 minerals would play the role of geochemical niches allowing for accumulation of biomolecules'  
42 precursors and protect them from UV radiation. In particular clays, as layered and charged materials,  
43 offer a large surface and a reactive environment which may have facilitated the organics' or  
44 biomolecules' synthesis, adsorption, and polymerization (Hazen and Sverjensky, 2010; Cleaves et al.,  
45 2012; Lambert et al., 2012; Rimola et al., 2013).

46 Adsorption of biomolecules and in particular nucleotides onto clays' surface has been extensively  
47 studied via experimental and theoretical approaches. For example, thirty years ago, Ferris investigated  
48 the adsorption of nucleotides onto (Al-Mg)-rich swelling clay montmorillonite (Ferris, 1989, 1993,  
49 2005), followed by a series of works with activated nucleotides, which showed that clay surface could  
50 catalyze the polymerization leading to RNA oligomers as long as 50-mers (Ferris, 2002). Recently,  
51 experimental studies investigated the adsorption of non-activated nucleotides onto clays under  
52 various environmental conditions, including mineral composition, pH, and salinity. The results showed  
53 that 5'-monophosphate deoxyribose and 5'-monophosphate ribose nucleotides behave in a similar  
54 way on the surface of Fe-Mg-rich and Al-rich phyllosilicates, independent of the nucleobase (Feuillie  
55 et al., 2013). Under conditions analogous to modern seawater, i.e. 0.5 M NaCl and 0.05 M MgCl<sub>2</sub>, and  
56 nearly neutral pH, a ligand exchange mechanism has been proposed with the phosphate group of the  
57 nucleotides binding the metal-hydroxyl groups of the edge surfaces of phyllosilicates (Pedreira-Segade  
58 et al., 2016). However, this adsorption mode tends to preclude further polymerization since a free  
59 phosphate group is mandatory to the formation of the phosphodiester bond that makes the backbone  
60 of oligonucleotides. The effect of various salts has been considered with swelling and non-swelling  
61 phyllosilicates (Pedreira-Segade et al., 2018). It was proposed that divalent cations (Mg<sup>2+</sup> or Ca<sup>2+</sup>) would  
62 preferably lead to cationic bridging adsorption on basal surfaces, *i.e.* through cation coordination by  
63 the negatively charged phosphate group. Interestingly, this mechanism indicates a higher retention  
64 capacity of the swelling clays compared to non-swelling phyllosilicates (Pedreira-Segade et al., 2018a).  
65 In agreement with the cation bridging mode by the phosphate group, combined experimental and  
66 computational approaches have shown that 5'AMP binds better onto montmorillonite as compared to

67 adenine and adenosine at high salts concentration solutions (Villafañe-Barajas et al., 2018). The effect  
68 of high concentrations of transition metal cations, potentially representative of the primitive ocean,  
69 on nucleotides adsorption has also been studied recently (Hao et al., 2018). It was observed that  
70 transition metal salts led to an increase of the adsorption up to twice or more for  $Zn^{2+}$  as compared to  
71  $Na^+$ . Moreover, clay composition and solution pH seem to have important influences on the  
72 adsorption, for all considered salts. Indeed, nontronite, a Fe-rich clay which carries negative charges in  
73 the surface tetrahedral layer (Al substituted  $SiO_2$  layer), displays a better nucleotide retention on its  
74 surface as compared to montmorillonite (Mg-rich), which carries negative charges in the sandwiched  
75 octahedral layer (Mg substituted  $AlO_3$  layer). A higher adsorption is observed at acidic pH=3 than at  
76 pH=7 for alkali and earth-alkali cations.

77 In the present study we aim at assessing the possible adsorption modes and molecular interactions  
78 responsible for the retention of nucleotides on clays' surface through classical molecular dynamics  
79 (MD) simulations. Various theoretical studies have addressed the interaction of biomolecules with  
80 mineral surfaces in order to describe and understand adsorption modes and reactivity (Rimola et al.,  
81 2013, 2019). In particular the study of adsorption of nucleobases on montmorillonite surface, via both  
82 static and dynamic DFT calculations, highlighted the possible physisorption modes (Mignon et al.,  
83 2009; Mignon and Sodupe, 2012, 2013). It suggested that nucleobases may bind through H-bonding  
84 perpendicular to the surface or through dispersion/Van der Waals interactions parallel to the surface.  
85 The interaction significantly increases when the nucleobase coordinates a cation, corresponding to the  
86 cation bridging adsorption mode. Potential adsorption through H-bonding was also possible at the  
87 hydroxylated edge clay surfaces (Mignon et al., 2019). In comparison with DFT calculations, classical  
88 MD simulations permit to considerably increase size and time scale of the system. Well parametrized  
89 force fields allow, with a reasonable accuracy, exploring more adsorption modes and assessing the  
90 affinity of the nucleobase for the mineral surface in conditions close to experimental ones. Only very  
91 few MD studies have been devoted to the adsorption of nucleotides on clay surfaces. Stacking  
92 interaction of adenine nucleobase on the surface was observed in a MD simulation of nucleotides in  
93 montmorillonite interlayer (Mathew and Luthey-Schulten, 2010). In the presence of  $Ca^{2+}$ , cation-  
94 phosphate coordination was observed, and it was argued that oligonucleotide may adsorb in the  
95 interlayer. This definitely requires further investigation since the primitive seawater composition may  
96 have been largely different from present-day : higher Ca, lower Mg, high Fe(II) and Mn(II) (Halevy and  
97 Bachan, 2017; Krissansen-Totton et al., 2018; Marty et al., 2018; Tosca et al., 2019), thus allowing  
98 interlayer cation exchange and the presence of divalent cations at the basal surface of clays. More  
99 recently MD simulations have highlighted other adsorption modes of nucleotides (Pedreira-Segade et  
100 al., 2018a) with a possibly preferential adsorption of GMP on the basal surface of montmorillonite in

101 presence of  $\text{Ca}^{2+}$  cations in solution. It was observed that the phosphate may coordinate to cations and  
102 the nucleobase interacts with the mineral surface directly through H-bonding or Van der Waals  
103 interactions. Following these investigations, we tackle in the present study the effect of environmental  
104 conditions on the adsorption of nucleotides by varying the pH, clay composition and salts in solution  
105 through classical MD modelling. The deoxyguanosine monophosphate (dGMP) nucleotide is  
106 considered as a model like in recent experiments (Hao et al., 2018; Pedreira-Segade et al., 2018b). Its  
107 different protonation states according to considered pKas are considered in order to mimic acidic and  
108 neutral pH. Nontronite and montmorillonite are the clay minerals investigated here; their difference  
109 in compositions allows to understand the role of surface charges on nucleotide adsorption. Finally, the  
110 effect of monovalent vs. divalent cations is assessed *via*  $\text{Na}^+$  or  $\text{Ca}^{2+}$  containing models.

### 111 **Computational Details.**

112 **Models.** Clay models have been built from the X-Ray data of pyrophyllite (Lee and Guggenheim, 1981),  
113 which has been refined through DFT calculations. Unit-cell dimension and atoms positions were  
114 optimized using the PBE functional through periodic plane waves calculations with the VASP package  
115 (Kresse and Hafner, 1993; Kresse and Furthmüller, 1996). Optimized cell parameters were very close  
116 to experimental ones (less than 2% variation):  $a=5.083\text{\AA}$ ,  $b=8.897\text{\AA}$ ,  $c=9.410\text{\AA}$ ,  $\alpha=90.12^\circ$ ,  $\beta=100.58^\circ$ ,  $\gamma=$   
117  $89.94^\circ$ . Since only one layer is considered in our model, the cell was changed to orthorhombic. In order  
118 to model the basal surface, the basic box was built by multiplying  $a \times 6$  and  $b \times 4$  leading to box basal  
119 dimensions:  $a=30.498\text{\AA}$  and  $b=35.588\text{\AA}$ . Clay composition was set according to previous experimental  
120 works (Feuillie et al., 2013; Hao et al., 2018). Montmorillonite composition:  $(\text{Si}_{7.95} \text{Al}_{0.05})(\text{Al}_{2.75} \text{Fe}^{3+}_{0.17}$   
121  $\text{Mg}_{1.07})\text{O}_{20} (\text{OH})_4 \text{Na}_{1.11}$  was modelled through 26 octahedral substitutions  $\text{Al}^{3+}$  by  $\text{Mg}^{2+}$ ; Nontronite  
122 composition  $(\text{Si}_{6.98} \text{Al}_{0.95} \text{Fe}^{3+}_{0.07})(\text{Al}_{0.36} \text{Fe}_{3.61} \text{Mg}_{0.04})\text{O}_{20} (\text{OH})_4 \text{Na}_{1.05}$  was approximated by including 24  
123  $\text{Si}^{4+}$  by  $\text{Al}^{3+}$  tetrahedral substitutions and 86  $\text{Al}^{3+}$  by  $\text{Fe}^{3+}$  octahedral substitutions; the latter not leading  
124 to any layer charges. Atomic substitutions were done randomly respecting the rule separation between  
125 octahedral substitutions: at least one octahedral center between two substitutions.  $\text{Na}^+$  counter-  
126 cations were included in solution according to the number of substitutions in the mineral layer.  $\text{Na}^+$ -  
127  $\text{Cl}^-$  pairs were added to the water molecules initially added to the system, in agreement with the  
128 experimental conditions of 0.5 M NaCl aqueous solutions (Hao et al., 2018).

129 The nucleotide geometries and charge parameters were refined through DFT calculation at the  
130 B3LYP/6-31G\* level. Nucleotides were optimized in the gas phase and then RESP atomic partial charges  
131 reproducing the electrostatic potential on a molecular surface have been used (Woods and Chappelle,  
132 2000). Two protonated states were considered for dGMP according to guanine's and phosphate's pKas  
133 (Shabarova and Bogdanov, 1994) and the selected pH value of the simulations (Figure 1). At acidic pH

134 close to pH=3, the phosphate group carries one negative charge while almost 50% of the aqueous  
135 guanine moiety is positively charged. At pH<3, guanine is protonated at N7 and the phosphate group  
136 carries one negative charge, referred as dG<sup>+</sup>mP<sup>-</sup>. At pH=7 guanine is neutral and the phosphate group  
137 carries two negative charges, it will be referred as dGmP<sup>2-</sup>. Figure 1 shows the geometries of the  
138 nucleotides.

139 The ClayFF force field was used for clay models (Cygan et al., 2004) while water and ions were modelled  
140 using the SPC/E and Dang models, respectively (Berendsen et al., 1981; Dang, 1995). The SPC/E model  
141 is known to accurately reproduce water structure. The General Amber Force Field (Wang et al., 2004)  
142 was used to generate nucleotide parameters and Lorentz-Berthelot rules were applied for inter force  
143 fields parameters. This approach has already been successfully used in various theoretical works  
144 (Thyveetil et al., 2008; Swadling et al., 2010, 2012, 2013). The Amber force field has been extensively  
145 used in nucleic acids modelling and reproduces well the structure and dynamics of nucleic acid moieties  
146 (Cheatham III and Young, 2000; Thyveetil et al., 2008; Swadling et al., 2010). Amber and ClayFF are  
147 rather simple to combine since both use harmonic potential for bond terms, although ClayFF uses  
148 neither angle nor dihedral terms. Periodic boundary conditions were applied in all three spatial  
149 directions.

150 The large-scale atomistic/molecular massively parallel simulator (LAMMPS) (Plimpton, 1995) was used  
151 for all simulations. A unique clay layer was considered to model the basal surface, and it was divided  
152 half at the bottom and top of the box along the z vertical parameter. The initial separation was set to  
153 60 Å, the nucleotide was placed in the center of the box, water molecules filled the empty space in a  
154 regular grid (with a 3.3 Å interval) including the amount of Na<sup>2+</sup>, Ca<sup>2+</sup> and Cl<sup>-</sup> needed to get a total  
155 neutral charge. A cutoff of 12 Å was applied to the electrostatic and Lennard-Jones interactions.  
156 Coulombic interactions were computed by Ewald summation and the particle-particle, particle-mesh  
157 method at a 0.0001 accuracy. All simulations were carried out at 300 K and 1 atm. The oxygen-  
158 hydrogen bonds of water molecules were maintained fixed by applying the shake algorithm (Ryckaert  
159 et al., 1977). The equilibration period consisted in warming up the system, starting from water/ions  
160 moiety then the clays particles and the nucleotide, successively, via the NVT ensemble. The system  
161 was then allowed to relax along all directions through the NPT ensemble. This step allowed to fix the  
162 vertical separation between basal surfaces for the whole production. The system was then  
163 equilibrating through two steps increasing the time step from 0.1 to 0.5 fs. The whole equilibration  
164 spent 800000 time steps. During the whole simulation and production, the octahedral atoms were  
165 maintained fixed. The production time during which data were analyzed was 100 ns for all simulations.

## 166 **Results and Discussion.**

167 In order to study the effects of mineral composition, pH and aqueous cations, simulations were  
168 performed through the same equilibration/production procedures for all systems. Mineral  
169 composition has been tackled by considering the montmorillonite and nontronite minerals; pH effect  
170 was studied with  $dGMP^{2-}$  and  $dG^+MP^-$  nucleotides at pH=7 and pH=3, respectively; and mono-/di-valent  
171 cations effects were investigated by adding 0.05M  $CaCl_2$  salt to the initial 0.5M NaCl solution.

172 **Mineral composition effect.** Density profiles along the z coordination are shown in Figure 2 for  $dGMP^{2-}$   
173 and  $dG^+MP^-$  nucleotides and both montmorillonite and nontronite minerals. The first and most  
174 distinctive property for both minerals is the  $Na^+$  cation density near clay surfaces. One notices a  
175 cationic structure made of three layers. For montmorillonite, the first peak is at 0.55 - 0.85 Å, the  
176 second at 2.55-2.75 Å, and the third one at 4.10-4.20 Å, representing 6.7-6.8 %, 7.4-11.1 % and 35.0-  
177 37.2 % of the total amount of aqueous cations in the system, respectively (data given for  $dGMP^{2-}$  and  
178  $dG^+MP^-$  nucleotides in Table 1). For nontronite, the values of peaks' positions and cations amount (in  
179 parentheses) are: 0.50-0.55 Å (19.0-19.3 %), 2.00-2.05 Å (32.2-32.4 %) and 4.20-4.25 Å (10.9-12.7 %).  
180 This shows that the first two peaks are closer to the surface of nontronite as compared to  
181 montmorillonite; the difference is striking for the second peak. The first two layers are also much more  
182 populated for nontronite, which contains 51.4-51.5 % of all aqueous cations, as compared to  
183 montmorillonite, whose cation density remains as low as 14.1-17.9 %. The total cation density near  
184 the surface is higher for nontronite than for montmorillonite: 62.4-64.1 % and 51.3-52.9 %,   
185 respectively. This difference is clearly due to the distribution of negative charges, which are located on  
186 the surface oxygen atoms of nontronite because of tetrahedral substitution as opposed to  
187 montmorillonite which negative charges are located on the internal oxygen atoms due to octahedral  
188 substitutions. The effects of this charge distribution are quite striking as almost the whole negative  
189 charge of the nontronite platelet is screened by cation; only 0.3 to 0.9 of the total 24.0 negative charges  
190 on the surface are not screened by  $Na^+$  cations. For montmorillonite, 5.1 to 6.0 negative charges are  
191 not screened over the 26.0 total negative charges. As a result, the negative charge is much less visible  
192 on nontronite surface from the bulk solution because of a much denser cation population in the first  
193 two layers above surface. It's also noticeable that the minimum density between the second and third  
194 cation layers for nontronite is well marked, showing a clear distinction between the third and the first  
195 two layers.

196 At pH=7, *i.e.* for  $dGMP^{2-}$ , the phosphate group of the nucleotide is found to be located at around 3.95  
197 Å above the surface oxygen atoms of nontronite for more than 61% of the simulation and at 6.90 Å for  
198 the remaining time. In addition, the O6 atom of guanine is located close to the nontronite surface at  
199 3.05 Å for more than 81% of the simulation. In comparison, the phosphate group remains further away  
200 from the montmorillonite surface at about 6.60-6.65 Å from the bottom and the top surfaces for 25.2%

201 and 60.2% of the simulation, respectively, representing 85.4% of the simulation. The nucleobase  
202 position related to phosphate's position is present at 3.25 Å from the montmorillonite surface during  
203 4.4 % of the simulation. According to the radial distribution function (rdf) between the P atom of the  
204 phosphate and Na<sup>+</sup> cations, the negatively charged phosphate coordinates almost two cations during  
205 the simulation on montmorillonite (N=1.84) and nontronite (N=1.83) (see Table 2 for coordination  
206 numbers and first peak maximum obtained from radial distribution analysis). The sodium cation is  
207 around 2.35 Å away from phosphate oxygen atoms. This result suggests a strong affinity of the -HPO<sub>4</sub><sup>2-</sup>  
208 group for cations and thus strong phosphate-cation coordination may explain the different behavior  
209 in nucleotide adsorption. Indeed, because of the layer structure of cations above clays' surface, the  
210 phosphate approaches the surface where most cations are located and screen the negative charge of  
211 the surface, thus alleviating electrostatic repulsion between clay's negative surface and the phosphate.  
212 For montmorillonite, the third cation layer at around 4.15 Å above the surface is the most populated.  
213 In this case, the phosphate tends to coordinate the cations of this layer, because the first two layers  
214 do not screen the negative charge of the surface due to low cation density. As such, the phosphate  
215 group remains at a distance of about 6.60 Å, which does not allow the nucleobase to approach close  
216 to the surface. At pH=7 guanine remains far from the surface of montmorillonite during most of the  
217 simulation at 6.15 - 8.45 Å (see Table 1) or interact through H-bonding as shown in Figure 3a, only 4.4%  
218 of the simulation. The results is different for nontronite, which negative surface charge is almost totally  
219 screened, and the first two cation layers are the most populated, thus responsible for most of charge  
220 screening. As a result, the phosphate approaches the cation layer and penetrates deeper to 3.95 Å  
221 from the surface (Table 1) and coordinate cations of the second layer that is the densest layer (Figure  
222 3b). The fact that the phosphate can approach close to nontronite's surface may allow the nucleobase  
223 to adsorb closely onto the surface, *i.e.* at 3.05 Å. At such a short distance from the nontronite's surface  
224 the nucleobase is engaged in planar adsorption mode with the surface to maximize Van der Waals  
225 interactions for more than 80% of the simulation (Figure 3b). Such an interaction between the  
226 nucleobase and the surface has already been observed in previous calculations, which showed that the  
227 base is stabilized through both Van der Waals interactions and cation coordination with O6 guanine  
228 atom (Mignon et al., 2009; Mignon and Sodupe, 2013). Although the coordination number is only 0.32,  
229 the guanine coordinated Na<sup>+</sup> cation is at a distance of 2.44 Å, thus showing a rather strong  
230 coordination.

231 **pH effect.** By comparing density profiles with dG<sup>+</sup>MP<sup>-</sup> and dGMP<sup>2-</sup> corresponding to pH=3 (Figure 2a &  
232 2b) and pH=7 (Figure 2c & 2d), respectively, we can evaluate the effect of the pH on nucleotide  
233 adsorption onto montmorillonite or nontronite. The most important difference between dG<sup>+</sup>MP<sup>-</sup> and  
234 dGMP<sup>2-</sup> arises from the adsorption of the nucleobase. Indeed, for montmorillonite, guanine remains



235 adsorbed on the surface for 33.4 % of the simulation at pH=3 whilst it is limited to 3.4 % at pH=7. For  
236 nontronite the difference is less pronounced; the nucleobase is adsorbed on the surface during the  
237 whole simulation at pH=3 and somehow less (81.2 %) at pH=7. The Na<sup>+</sup> coordination by O6 is also less  
238 important for dG<sup>+</sup>MP<sup>-</sup>; the coordination number is less than 0.2 with a larger O6-Na<sup>+</sup> distance between  
239 2.46 and 2.48 Å, as compared to p=7 (see Table 2 for coordination numbers and first peak maximum  
240 obtained from radial distribution analysis). Finally, and most importantly, the coordination of the  
241 phosphate toward Na<sup>+</sup> is almost negligible at pH=3, coordination numbers and first peak maximum  
242 distances are 0.04/3.16 Å and 0.14/3.63 Å for montmorillonite and nontronite, respectively, as  
243 compared to 1.84/3.04 Å and 1.83/3.06 Å at pH=7. This shows that the nucleotide adsorption at pH=3  
244 is obviously not due to the electrostatic interaction between the phosphate and Na<sup>+</sup> cations organized  
245 in layers above the surface; at pH=3 the phosphate group carries only one negative charge. At pH=3  
246 nucleotide adsorption is due the attraction of the positively charged guanine nucleobase by the  
247 negative surface charges, leading to a very strong adsorption onto the clay surface (Figure 4). In  
248 contrast adsorption pH=7 is due to phosphate interactions with Na<sup>+</sup> surface layers allowing for the  
249 nucleobase to approach the surface being stabilized through Van der Waals interactions.

250 **Salts effects.** The effect of divalent cations has been tackled by adding Ca<sup>2+</sup> cation in solution at two  
251 concentrations, at pH=7 and evaluating the effect on the adsorption onto nontronite surface. The first  
252 low concentration of 0.05 M CaCl<sub>2</sub> is equivalent to that used experimentally (Hao et al., 2018), and  
253 corresponds to 2 additional Ca<sup>2+</sup> cations in the simulation box. The effect of the added Ca<sup>2+</sup> cations was  
254 not clearly visible during the time given for the simulation; 2 Ca<sup>2+</sup> among 37 Na<sup>+</sup> do not allow to observe  
255 any change in the layers above clay surface. The second concentration is equivalent to a 0.25 M CaCl<sub>2</sub>  
256 solution, is higher than that used by Hao et al. (2018) and allows to observe the effect of Ca<sup>2+</sup> cations  
257 in our model. This concentration corresponds to 7 additional CaCl<sub>2</sub> in the simulation box, and the only  
258 Na<sup>+</sup> cations present are counter cations due to substitutions' charge compensation. Such a high  
259 concentration is still relevant for the early seawater (Halevy and Bachan, 2017; Krissansen-Totton et  
260 al., 2018). Firstly, we observe that one Ca<sup>2+</sup> cation is almost always coordinated to the phosphate  
261 group, showing the very high affinity of Ca<sup>2+</sup> for the -PO<sub>4</sub><sup>2-</sup> group. Coordination numbers and distances  
262 (computed from the P-Ca radial distribution function, Table 2) are 0.88/2.87 Å and 0.98/2.93 Å for low  
263 and high Ca<sup>2+</sup> concentration, respectively. One may notice the low coordination numbers and large  
264 distances between Na<sup>+</sup> and P (computed from P-Na<sup>+</sup> rdf), 0.26/3.60 Å at high Ca<sup>2+</sup> concentration. This  
265 shows that Na<sup>+</sup> cation is absent in the first phosphate coordination sphere when a Ca<sup>2+</sup> is coordinated  
266 to the nucleotide phosphate moiety. Thus in presence of a divalent cation, the coordination of  
267 phosphate with cations is almost exclusive.

268 Density profiles for both systems are shown in Figure 5. For the low  $\text{Ca}^{2+}$  concentration system, only a  
269 few configurations have been sampled when  $\text{Ca}^{2+}$  cations have been found in the 2<sup>nd</sup> cation layer, and  
270 half a  $\text{Ca}^{2+}$  cation is found in the third layer, statistically over the simulation. As a result, the phosphate  
271 group remains rather far from the surface mainly at 5.15 and 5.85 Å (Table 3). However, this does not  
272 prevent the guanine from strongly binding the surface; it adsorbs the surface at 3.05 Å for 85 % of the  
273 simulation in a parallel configuration as shown in Figure 7a. For the high concentration system, 1-2  
274  $\text{Ca}^{2+}$  and 0.6-1.2  $\text{Ca}^{2+}$  can be found in the second and third cation layers above the surface, respectively.  
275 As above-mentioned, the high  $\text{Ca}^{2+}$  concentration allowed to sample more the 2<sup>nd</sup> layer  $\text{Ca}^{2+}$  cation  
276 exchange configurations, in agreement with experiments over a longer time scale. The 2<sup>nd</sup> layer cation  
277 exchange by divalent cation, mainly coordinated to the phosphate group allows the phosphate to  
278 approach closer to the surface as shown by a high density (50.1 %) of the phosphate group at 3.30 Å  
279 only of the surface (Table 3). This distance corresponds to the shortest distance between the  
280 phosphate and the surface among all the simulations run in the present study. As a result, one can see  
281 that the nucleotide density is almost entirely (91.2 %) located at 3.15 Å, which corresponds to a planar  
282 adsorption of the nucleotide of the surface, thus maximizing the Van der Waals interaction (Figure 7b).

### 283 **Conclusion.**

284 The classical MD simulations carried out in this study allowed us to investigate the effect of mineral  
285 composition, pH, salinity, and salt concentration on nucleotide adsorption onto clay surfaces. Mineral  
286 composition has substantial effects on nucleotide adsorption.

287 First, we observed that cations close to the negatively charged surface are structured in three layers  
288 above the surface at about 0.5-0.8 Å, 2.0-2.7 Å and 4.1-4.2 Å, respectively. The layers' density may  
289 change as function of mineral composition and charge location on their basal surface. If the charge is  
290 located in the octahedral (inner) clay layer, the two first cations layers are less populated while the  
291 third layer comprises most cations. If the negative charge is located in the tetrahedral layer just in  
292 contact with solutes, the first two cations layers concentrates the majority of the aqueous cations. As  
293 a result, the negative surface charge is screened and the negatively charged nucleotide phosphate  
294 group can coordinate cations preferentially in the most populated cation layer. This screening allows  
295 the nucleobase to bind the surface in a coplanar configuration, maximizing Van der Waals interactions.  
296 Secondly, at acidic pH protonated species due to the protonation of guanine N7 site at pH=3 for  
297 instance, may bind the negatively charged clay surface through electrostatic (and Van der Waals still  
298 present) interactions. Moreover, in that case the adsorption is completely driven by this interaction;  
299 no phosphate-cation coordination was observed at this low pH. This again shows the importance of  
300 the negative surface charge towards adsorption. Finally, the effect of the aqueous divalent cations is

301 found to be preponderant since the  $-\text{PO}_4^{2-}$  group does coordinate exclusively these divalent cations. As  
302 a result, due to cation exchange and the presence of these cations in the layers' structure above the  
303 surface, the phosphate group approaches very close to the mineral surface through strong cation  
304 coordination and allows nucleobase binding. The effect of cations is predominant toward nucleotide  
305 adsorption while it may be tuned by varying mineral composition and pH; the effect of the latter  
306 potentially involving a different adsorption mode, driven by different molecular interactions.

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**Table 1.** Density profiles data corresponding to Figure 2. Peaks' distances from top or bottom surface oxygen atoms are given in Å and their integral are given in percentage of the number of the considered atoms (Na<sup>+</sup>, O6, P) present in the simulation box

			Os - Na <sup>+</sup>			Os - O6	Os - P
			1rst layer	2nd layer	3rd layer		
pH = 3	Montmorillonite	Top surface	0.85 (2.7)	2.55 (4.1)	4.20 (20.2)	-	-
		Bottom surface	0.55 (4.0)	2.60 (3.3)	4.10 (17.0)	2.95 (33.4) - 5.60 (18.5)	6.90 (24.8) - 10.35 (35.3)
	Nontronite	Top surface	0.50 (8.9)	2.05 (18.5)	4.20 (6.0)	3.15 (49.5)	6.65 (54.3)
		Bottom surface	0.50 (10.4)	2.00 (13.7)	4.20 (4.9)	3.15 (41.5)	6.55 (41.3)
pH = 7	Montmorillonite	Top surface	0.80 (3.2)	3.75 (7.7)	4.20 (17.9)	3.25 (4.4) - 6.15 (10.3) - 8.45 (14.0)	6.65 (60.2)
		Bottom surface	0.55 (3.6)	2.55 (3.4)	4.15 (17.1)	-	6.60 (25.2)
	Nontronite	Top surface	0.50 (8.6)	2.05 (17.6)	4.20 (5.8)	-	-
		Bottom surface	0.55 (10.4)	2.05 (14.8)	4.25 (6.9)	3.05 (81.2) - 10.25 (10.9)	3.95 (61.2) - 6.9 (26.9)

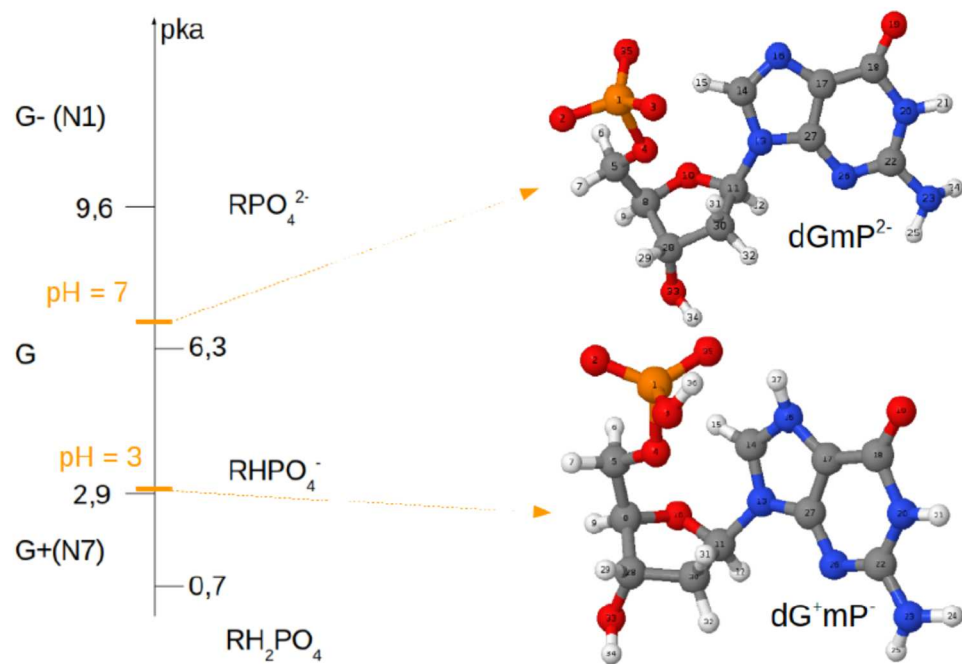
**Table 2.** Coordination data obtained from radial distribution function analysis. First peak maximum distances given in Å.

Salt	nucleotide	Clay	P-Na		O6-Na		P-Ca		O6-Ca	
			Coord. Nb	dist.	Coord. Nb	dist.	Coord. Nb	dist.	Coord. Nb	dist.
NaCl	dG <sup>+</sup> mP <sup>-</sup>	MNT	0,04	3,16	0,20	2,46				
		NNT	0,14	3,63	0,17	2,48				
	dGmp <sup>2-</sup>	MNT	1,84	3,04	0,35	2,44				
		NNT	1,83	3,06	0,32	2,44				
NaCl + CaCl <sub>2</sub> [0,05 M]	dGmp <sup>2-</sup>	NNT	0,48	2,38	0,37	2,43	0,88	2,87	0,02	2,40
CaCl <sub>2</sub> [0,25 M]		NNT	0,23	3,60	0,19	2,42	0,98	2,93	0,01	2,43

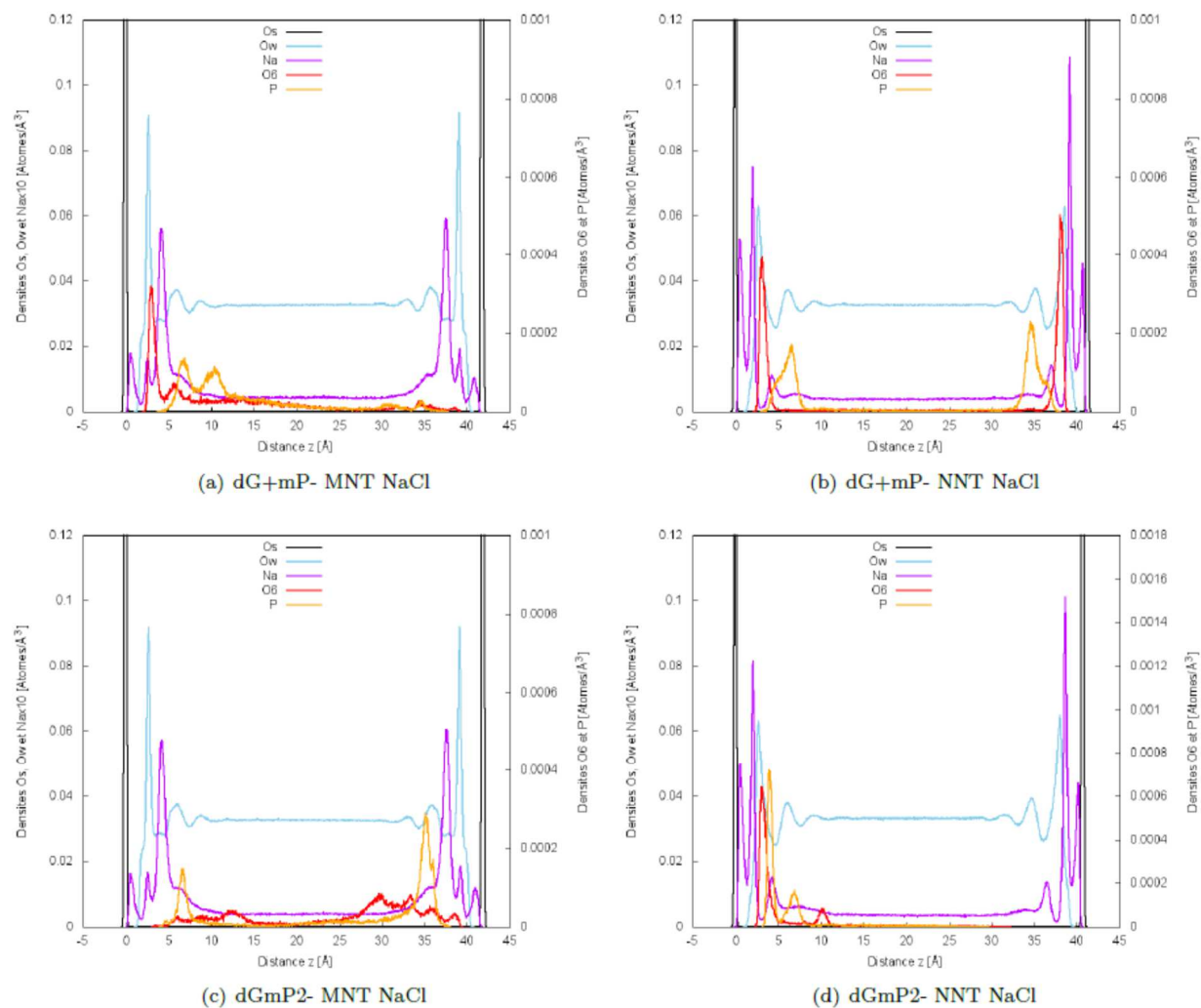
**Table 3.** Density profiles data corresponding to Figure 4. Peaks' distances from top or bottom surface oxygen atoms are given in Å and their integral are given in percentage of the number of the considered atoms (Na<sup>+</sup>, O6, P) present in the simulation box

		Os - Ca <sup>2+</sup>			Os - O6	Os - P
		1rst layer	2nd layer	3rd layer		
NaCl [0.5] + CaCl <sub>2</sub> [0.05]	Top surface	-	-	4.30 (1.8)	-	-
	Bottom surface	-	2.20 (14.9)	4.25 (27.8)	5.05 (85.8)	5.15 (32.9) - 5.85 (57.3)
CaCl <sub>2</sub> [0.25]	Top surface	-	2.05 (28.7)	4.25 (8.8)	-	-
	Bottom surface	-	2.15 (13.7)	4.25 (17.2)	3.15 (91.2)	3.30 (50.1) - (5.70 (16.6) - 6.05 (25.3)

**Figure 1.** Protonation states of dGmP as a function of pH and pKas (Shabarova and Bogdanov, 1994).

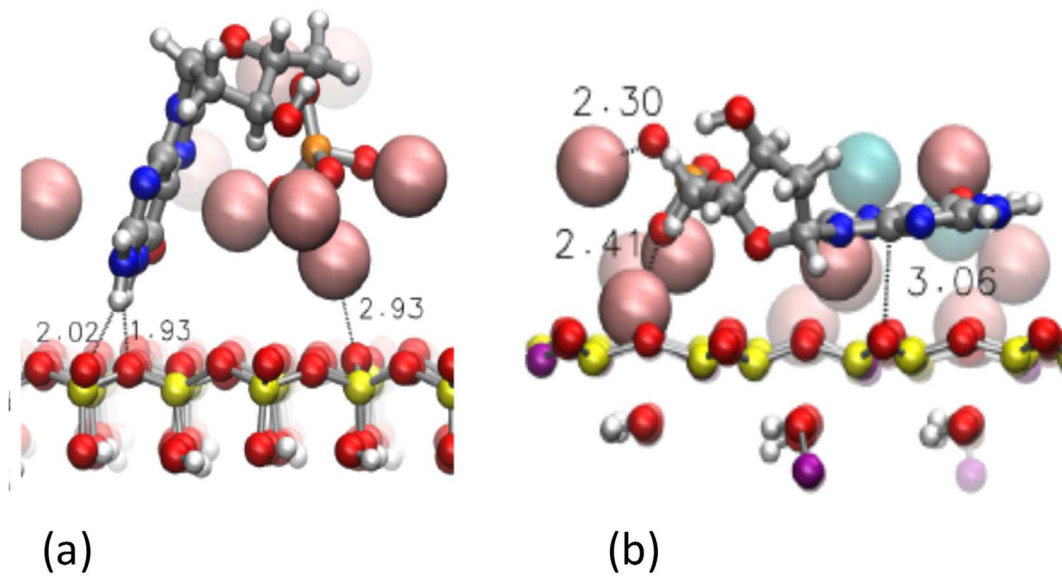


**Figure 2.** Density profiles along z coordinate for a)  $dG^+mP^-$  with montmorillonite, b)  $dG^+mP^-$  with nontronite, c)  $dGmP^{2-}$  with montmorillonite, d)  $dGmP^{2-}$  with nontronite. Surface oxygen atoms  $O_s$  are depicted in black, water oxygens in blue,  $Na^+$  cations in pink,  $O6$  of guanine and  $P$  of the phosphate group of the nucleotide in red and orange respectively.

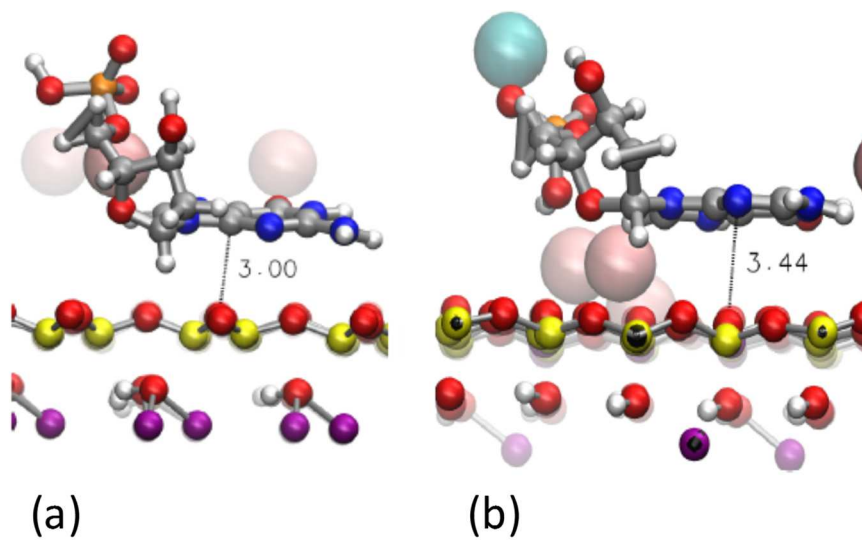




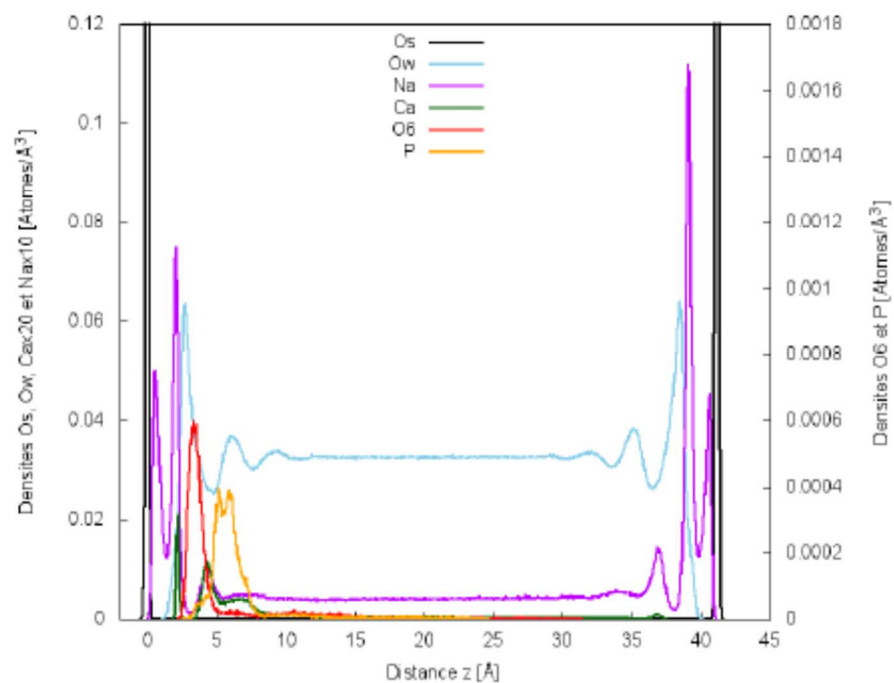
**Figure 3.** Snapshots of (a) dGmp<sup>2-</sup> adsorbed on montmorillonite surface, and (b) on nontronite surface. Distances are given in Å.



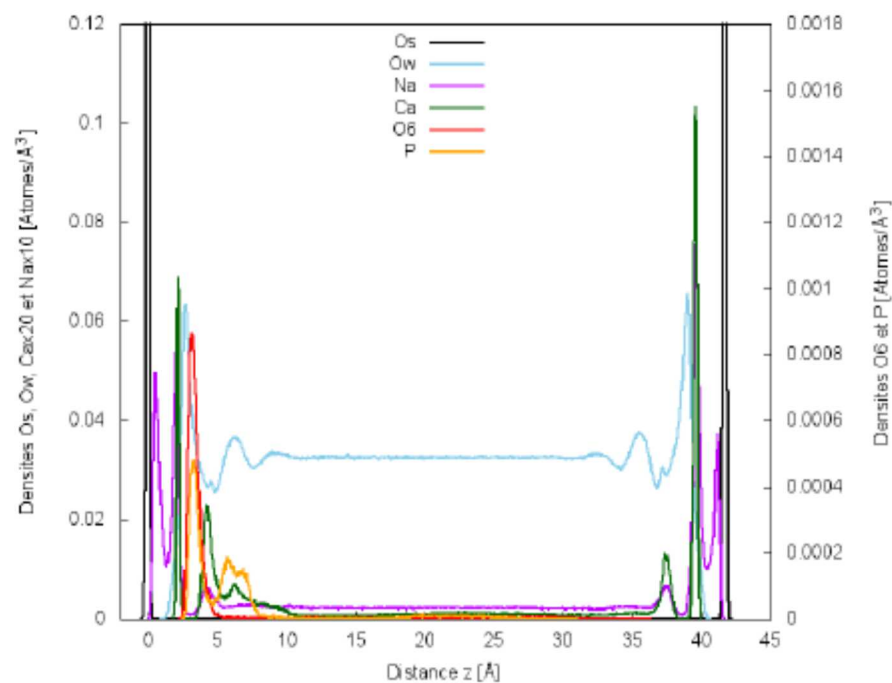
**Figure 4.** Snapshots of (a)  $dG^{+}mp^{-}$  adsorbed on montmorillonite surface, and (b) on nontronite surface. Distances are given in Å.



**Figure 5.** Density profiles along z coordinate for dGmP<sup>2-</sup> with nontronite at a) low [0.05M ] CaCl<sub>2</sub> concentration, b) at high [0.25 M] CaCl<sub>2</sub> concentration. Surface oxygen atoms Os are depicted in black, water oxygens in blue, Na<sup>+</sup> cations in pink, Ca<sup>2+</sup> in green, O6 of guanine and P of the phosphate group of the nucleotide in red and orange respectively.

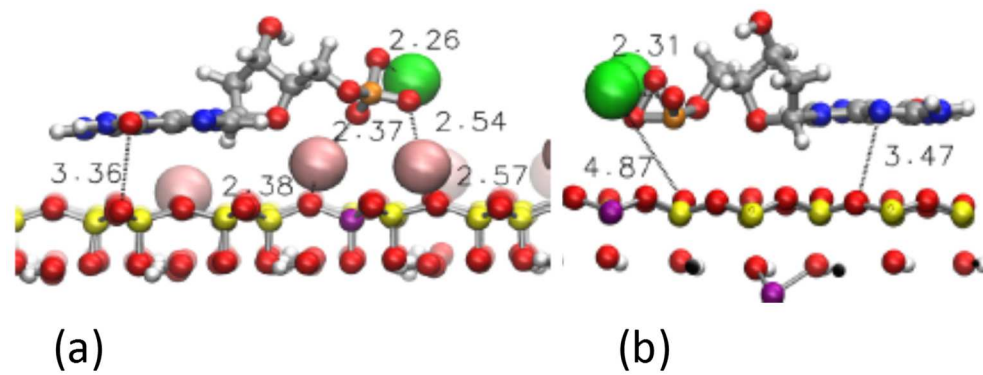


(a) dGmP<sub>2</sub>- NNT NaCl+CaCl<sub>2</sub>



(b) dGmP<sub>2</sub>- NNT CaCl<sub>2</sub>

**Figure 7.** Snapshots dGmp<sup>2-</sup> adsorbed on nontronite surface at (a) low and (b) high Ca<sup>2+</sup> concentrations. Distances are given in Å.



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