Design of Ceramics with Strong Adhesion to RNAs and Peptides with an Efficient Materials Informatics Technology

by

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Appropriate ceramics with strong adhesion to single-stranded ribonucleic acids (RNAs), which are used in biomedical and electronic devices, was selected by using an efficient materials-informatics technology based on a combination of an orthogonal array and a response-surface method. In this technology, at the first stage, important factors that significantly influence the adhesion strength were selected from various factors that characterize ceramic materials by using an orthogonal array with molecular simulations. As a result, the short-side and long-side lattice constants \( a \) and \( b \) were selected from four ceramic-material factors \( (a, b, \text{surface energy density}, S, \text{and the cohesive energy}, C) \). At the second stage, the adhesion strength was described as a function of the selected important factors by using a response-surface method. From this function, the optimal solution (the best values for \( a \) and \( b \)) that made the adhesion strength maximum were obtained. The best values for \( a \) and \( b \) were obtained as 0.338 nm and 0.585 nm, respectively. At the third stage, the best ceramic material whose lattice constants were equal to the best values \( (a=0.338 \text{ nm and } b=0.585 \text{ nm}) \), which are the lattice constants of single-stranded RNA, was selected by use of the simulation results of lattice constants. As a result, \( \text{CaO-9\%MgO, ZrO}_2-37\%\text{MgO and HfO}_2-28\%\text{MgO} \), whose lattice constants were \( a=0.338 \text{ nm and } b=0.585 \text{ nm} \), were selected as the best ceramic materials with the strongest adhesion to RNA. By applying the same technology to another application (the design of the ceramic material with strongest adhesion to a peptide that is a small part of proteins), \( \text{CaO-9\%NiO, ZrO}_2-34\%\text{NiO, and HfO}_2-26\%\text{NiO} \), whose lattice constants were close to peptide’s values \( (a=0.336 \text{ nm and } b=0.582 \text{ nm}) \), were selected.

Key words:
Adhesion strength, Ceramics, RNA, Peptide, Molecular simulation, Materials informatics

1 Introduction

Ribonucleic acids (RNAs) and deoxyribonucleic acids (DNA) are used to detect disease-causing viruses in biomedical technologies such as polymerase chain reaction (PCR)
, and they are also used as biodegradable functional materials in electromechanical technologies
. Before using RNAs and DNAs in biomedical devices, it is needed to collect a lot of RNAs and DNAs by attaching RNAs to adhesive materials such as ceramic membranes and ceramic beads
, which are set in extraction columns. When the adhesion strength is not sufficiently strong, only small amount of RNAs and DNAs can be collected, and the detection accuracy becomes low. So, the adhesion of RNAs and DNAs to ceramic membranes and beads is important in efficiently collecting RNAs and DNAs. The adhesion strength is also important in improving the reliability of biomedical and electronic devices where RNAs and DNAs are used as biodegradable functional materials
, following the trend towards eco-friendly products. For these reasons, the author tried to design the best ceramic material with strong adhesion to RNAs and DNAs by using materials-informatics (MI) technology based on a combination of an orthogonal array
, with the response- surface method
. This paper describes the adhesion of ceramics to single-chain biomolecules (RNAs and peptides), while the adhesion to DNAs that are double-chain structures, i.e., double-helix structures are reported in another paper
.

Generally, it is difficult to select an appropriate material that has strong adhesion to another material by using a conventional trial-and-error approach. So, by combining an orthogonal array
 with the response- surface method
, the author has developed a materials informatics (MI) technology for efficiently selecting an inorganic material with strong adhesion to an organic material (RNA, DNA or a resin). This paper describes the application of this technology to the selection of a ceramic material that has strong adhesion to single-chain biomolecules (RNAs and peptides).

In the technology that the author has developed, at the first stage, the important factors that significantly influence the adhesion strength are selected from ceramic-material factors such as lattice constants and surface energy density that characterize ceramic materials by using an orthogonal array
 and molecular simulations
. At the second stage, by using a response-surface method
, the adhesion strength is described as a function of the selected important factors, and the most appropriate values (optimal solutions) of the factors that make the adhesion strength maximum are obtained. At the third (final) stage, appropriate ceramic materials whose factors are close to the most appropriate values are selected. In this study, the author designed ceramics with strong adhesion to single-chain biomolecules (RNAs and peptides).
2 Material-Design Technology

2.1 Material-Design Technology Made of Three Stages

The basic idea of material design in the author’s technology shown in Fig. 1 is to select a material whose factors $A, B, C, \cdots$ are close to the most appropriate values $A_{0}, B_{0}, C_{0}, \cdots$ that optimize an objective material property, $F$, by describing the property as a function of material factors (i.e., $F(A, B, C, \cdots)$). In this study, the objective material property, $F$ that the author wants to optimize is the adhesion to RNA, and the factors $A, B, C, \cdots$ that the author focus on are the lattice constants (geometrical factors), the surface energy density, and the cohesive energy of a ceramic material (energetic factors).

To describe the material property $F$ as a function of material factors $A, B, C, \cdots$, a number of data of experiments or simulations to interpolate are needed. If too many factors are used, a lot of data are needed for interpolation and it takes too much time to obtain the function $F(A, B, C, \cdots)$. So the author uses orthogonal-array analysis$^{9}$ to select only the important, dominant factors that strongly influence the adhesion to RNA, that is, objective material property.

The overview of the material-design technology is shown in Fig. 1. This figure shows that the method consists of three stages. At the first stage, by using the orthogonal-array sensitivity analysis$^{9}$ with molecular simulations$^{9}$, the important material factors that significantly influence an objective material property are selected from material factors (the lattice constants, the surface energy density, and the cohesive energy) that characterize ceramic materials. In sensitivity analysis, the results of molecular simulations of the objective material property that is paid attention to are used as input data. At the second stage, the objective material property, which is the adhesion to RNA in this paper, is described as a function of the selected important factors by using a response-surface method$^{9}$ with the molecular-simulation results that are also used at the first stage. By using this function, the most appropriate values of the factors that optimize the objective material property, which is adhesion strength between ceramics and RNA in this paper, are determined. At the third (final) stage, the materials (ceramic materials, in this paper) whose factors are close to the most appropriate values are selected.

2.2 Simulations Used at the First and Second Stages

As shown in Fig. 1, molecular simulations are used in the first and second stages. So the method of the simulations is explained in this section. The simulation model of RNA, which is used as a probe in microarrays, is shown in Figs. 2 and 3. The interbase spacing of RNA is 0.338 nm. Figure 2 shows an overview of RNA, where the schematic structures of bases (guanine, cytosine, adenine, and uracil) are shown. Figure 3 shows the details of the lattice structure of RNA, and the lattice constants. The simulation model that the author used in this study is an interface between RNA (Figs. 3 and 4) and a ceramic multilayer, as shown in Fig. 4. By using the ceramic multilayer made up of atomic-scale thin films shown in Fig. 4, instead of using a single ceramic material, it was possible to control the lattice constants of the top layer shown in Fig. 5 almost freely. To control the lattice constants, the author appropriately selected three ceramic materials (Ceramics 1, 2, and 3), as shown later in Table 3. On the other hand, it was difficult to control them by applying strain to
Fig. 3 Molecular structure and lattice constants of RNA (hydrogen atoms not shown in 3D visualization).

Fig. 4 Attached state of RNA and a ceramic multilayer.

Single ceramics because phase transition was caused by the strain. This is the reason that three-layer model is employed in this study. This simulation model was made by using "Materials Studio®" software from Dassault Systemes BIOVIA. Four RNA molecules, one of which is shown in Fig. 3, were used as a RNA model.

Next, the size of the ceramic-multilayer model shown in Fig. 4 is explained in this paragraph. From the past molecular dynamics simulations(9), it was found that the adhesion strength between organic and inorganic materials was almost independent of the thickness when the thickness was larger than 2 nm. So, in this study, the author set the thickness of the ceramic layer at 3 nm. The thickness of Ceramics 1, 2, and 3 in Fig. 4 was set at 1 nm. These values were determined to make it easy to control the lattice constants of the top layer of the ceramic multilayer. The sizes of the ceramics in the x and y directions are set at 10 nm and 10 nm, which are large enough for attachment of four RNA molecules.

In this study, the adhesion strength was evaluated by calculating the adhesive fracture energy(9) that was defined as the difference between the area density of potential energy of the RNA/ceramics-attached state (Fig. 5) and that of the RNA/ceramics-detached state. In this method, assuming that the adhesive fracture is quasi-static, the author neglect the difference between the energy of the RNA/ceramics-detached state and that of the transition state with the highest energy, because the difference is smaller than 1% of the adhesive fracture energy. The fracture energy was calculated by using molecular dynamics with a universal force field(9). The temperature was kept at 20° C by using a velocity-scaling method(9).

As described in Ref. 9), the universal force field used in molecular dynamics simulations is determined based on the element, its hybridization, and its connectivity. As explained in this reference, the potential energy of this force field is expressed as a sum of valence or bonded interactions and nonbonded interactions in the following equation.

\[
P = P_b + P_\gamma + P_o + P_{\text{ele}} + P_{\text{vdw}} \tag{1}
\]

Here, bond stretching \((P_b)\), bond angle bending \((P_\gamma)\), dihedral angle torsion \((P_o)\), and inversion terms \((P_{\text{ele}})\) are valence interactions. On the other hand, van der Waals \((P_{\text{vdw}})\) terms and electrostatic \((P_{\text{ele}})\) terms are nonbonded interactions. The universal force field expressed by Eq. (1) was employed in this study because the results obtained with this force field were confirmed to agree well with the results obtained with first principle quantum simulations (density-functional-theory simulations) by using the software, Dmol3, from Dassault Systemes BIOVIA. The results of the quantum simulations will be discussed in the next paper.

The electrostatic \((P_{\text{ele}})\) terms in Eq. (1) are long-range Coulomb interactions induced by the partial charges. So, the atoms were kept free to move, and no periodic boundary conditions are set so that long range electrostatic forces from the replica molecular models induced by the periodic boundary conditions do not influence real molecular models.
2.3 Material Factors Used at the First Stage

In this section, the material factors of ceramics are explained. The author focused on four factors (the short-side and long-side lattice constants, \(a\) and \(b\), the surface energy density, \(S\), and the cohesive energy, \(C\)) of the ceramic multilayer, and then investigated which factors significantly influence the adhesion strength. The lattice constants, \(a\) and \(b\) are defined at the top surface of the ceramic multilayer, as shown in Fig. 4. In this study, the \(x\)-plane in Figs. 4 and 5 is set parallel to the crystal plane of highest atomic density. The energetically stable crystal plane is most likely to appear at the surfaces when ceramic films are deposited by using physical vapor deposition (PVD). For example, by using PVD, the author obtained single-orientation films such as cubic \(\text{ZrO}_2(111)\), cubic \(\text{HfO}_2(111)\), cubic \(\text{CaO}(111)\), hexagonal \(\text{Al}_2\text{O}_3(0001)\), and cubic \(\text{SrO}(111)\) films. The short-side and long-side lattice constants \(a\) and \(b\) are defined at the crystal planes of the top ceramic layer, as shown in Fig. 5. On the ceramic layer, RNA is placed parallel to the surface so that the structure is energetically stable.

The surface energy density of the ceramics, \(S\), which is the energy density required to create a surface from bulk, was defined as half of the difference between the area density of potential energy of the surface-absent state and that of the surface-created state, where two surfaces are created by separating the surface-absent state. \(S\) was calculated by using molecular dynamics with a universal force field\(^{11}\).

The cohesive energy, \(C\), is defined as the difference between the potential energy of the free atoms and that of the atoms of a solid.

2.4 Orthogonal Array Used at the First Stage

At the first stage of the material-design technology (Fig. 1), the important material factors (ceramic factors) that significantly influence the objective material property (adhesion strength) are selected by clarifying the dependence of the adhesion strength on the four ceramic factors. When we investigate the dependence, we usually change the value of one factor with the other three factors fixed. However, it is time-consuming to clarify the dependence by using this method. Accordingly, the author used the orthogonal-array design methodology\(^{20}\), which is known to be effective for efficiently designing macro-scale structures such as propeller fans and diaphragms. In this methodology, when there are four material factors, only nine simulations or experiments shown in an L9 orthogonal array (see Table 1) are needed to clarify the important factors on which the adhesion strength strongly depends\(^{20}\). Here the author set Level 1 (small values), Level 2 (middle values), and Level 3 (large values) of the four factors at the regions shown in Table 2. Because each column in Table 1 (L9) contains three sets of three levels, the location of nine simulation points is considered to be balanced in the four-dimensional design space, and it is easy to consider statistical calculations\(^{20}\). The author set three levels so that each level has about one third of the ceramic-material simulation samples by using the results of molecular dynamics simulations. By looking into the data of molecular dynamics simulations, the author was able to find nine ceramic multilayers that correspond to the nine sets of factors shown in Table 1. These nine ceramic multilayers are shown in Table 3. When it is impossible to set three levels for each factor, the orthogonal array cannot be used. In such a case, the first stage in Fig. 1 has to be skipped, and all the factors have to be dealt with at the second stage, where more data than those of orthogonal array are needed for interpolation. By using the nine ceramic multilayers shown in Table 1 (i.e., Table 3), the sensitivity\(^{6}\) for the adhesive fracture energy\(^{6}\) between the ceramic multilayer and the RNA molecules was calculated. By applying sensitivity analysis\(^{21}\) based on orthogonal arrays to the fracture-energy data calculated for the nine ceramic multilayers in Table 1 (i.e., Table 3), the sensitivity of Level \(j\) of the \(i\)-th factor, \(W_j\) is given by

\[
W_j=10 \log [(P_j-Q_j)/n],
\]

where

\[
P_j=(D_{a1}+D_{a2}+\cdots+D_{an})/n \quad \text{and}
\]

\[
Q_j=(D_{b1}^2+D_{b2}^2+\cdots+D_{bn}^2-P_j)/(n-1).
\]

Here, \(D_{ab}\) is the \(k\)-th fracture-energy datum that belongs to Level \(j\) of the \(i\)-th factor, and \(n\) is the number of the data that belong to Level \(j\) of the \(i\)-th factor.

Table 1  L9 orthogonal array in the case of four factors.

| Condition | 1st factor: Short-side lattice constant \(a\) (nm) | 2nd factor: Long-side lattice constant \(b\) (nm) | 3rd factor: Surface energy density \(S\) (J/m²) | 4th factor: Cohesive energy \(C\) (10^9 J/mol) |
|-----------|--------------------------------------------------|--------------------------------------------|---------------------------------|-----------------------------------|
| 1 Level 1 | Level 1                                           | Level 1                                   | Level 1                         | Level 1                           |
| 2 Level 1 | Level 1                                           | Level 2                                   | Level 2                         | Level 2                           |
| 3 Level 1 | Level 3                                           | Level 3                                   | Level 3                         | Level 3                           |
| 4 Level 2 | Level 1                                           | Level 1                                   | Level 2                         | Level 3                           |
| 5 Level 2 | Level 2                                           | Level 3                                   | Level 3                         | Level 1                           |
| 6 Level 2 | Level 3                                           | Level 1                                   | Level 2                         | Level 3                           |
| 7 Level 3 | Level 1                                           | Level 3                                   | Level 2                         | Level 3                           |
| 8 Level 3 | Level 2                                           | Level 1                                   | Level 3                         | Level 2                           |
| 9 Level 3 | Level 3                                           | Level 2                                   | Level 1                         | Level 1                           |

Table 2  Factors and levels for ceramic multilayers.

| Parameter | 1st parameter: Short-side lattice constant \(a\) (nm) | 2nd parameter: Long-side lattice constant \(b\) (nm) | 3rd parameter: Surface energy density \(S\) (J/m²) | 4th parameter: Cohesive energy \(C\) (10^9 J/mol) |
|-----------|--------------------------------------------------|--------------------------------------------|---------------------------------|-----------------------------------|
| Level 1 (small) | \(a<0.3\)                                      | \(b<0.52\)                             | \(S<3.0\)                       | \(C<6.0\)                         |
| Level 2 (middle) | \(0.30 \leq a \leq 0.40\)                      | \(0.52 \leq b \leq 0.69\)               | \(0.8 \leq S \leq 1.8\)        | \(6.0 \leq C \leq 12.0\)          |
| Level 3 (large) | \(0.40 \leq a \leq 0.69\)                      | \(5.0 \leq S \leq 9.0\)                 | \(9.0 \leq C \leq 12.0\)       | \(9.0 \leq C \leq 12.0\)          |
According to the sensitivity-analysis method\(^1\) based on orthogonal arrays, the factors whose increase from Level 1 to Level 3 significantly influences the sensitivity \(W_0\) are important in maximizing the adhesion strength, and they are selected as important factors at the first stage of the material-design technology (Fig. 1). At the second stage in Fig. 1, the adhesion strength is described as a function of the selected factors by interpolating the nine fracture-energy data corresponding to the L9 orthogonal array in Tables 1 and 3 by use of a response-surface method.

### 2.5 Response-Surface Method

At the second stage of the material-design technology (Fig. 1), a response-surface method is used to describe the objective material property (adhesion strength) as a function of the important factors selected by use of the orthogonal-array analysis explained in Section 2.4. In this study, the author employed a response-surface method\(^6\), so called Kriging method, which is often used in geostatistics and mechanical structure design. The overview of one-dimensional data interpolation by use of the Kriging method is shown in Ref. 8), where the function curve is made so that all the data points used for interpolation are on the curve. The basic idea of the Kriging method is to predict the value of a function at a given point by computing a weighted average of the known values of the function in the neighborhood of the point. The theory derives a best linear unbiased estimator, based on assumptions on covariances, and is mathematically related to regression analysis.

By using the Kriging method, the adhesion strength with RNA is described as a function of the important material factors (ceramic-multilayer factors). By using this function, the most appropriate values of material factors that maximize the adhesion strength can be determined. At the third (final) stage, appropriate materials (ceramic multilayers) whose factors are close to the most appropriate values are selected.

### 3 Material-Selection Results and Discussions

The calculated adhesive fracture energy data corresponding to the L9 orthogonal array (Table 3) are shown in Table 4. Figure 6 shows the sensitivity \(W_0\) calculated by using the fracture energy data (Table 4) and Eqs. (2), (3), and (4). From Fig. 6 it is found that the adhesive fracture energy (adhesion strength) strongly depends on the 1st and 2nd factors (the short-side and long-side lattice constants), while the fracture energy does not strongly depend on the 3rd and 4th factors (the surface energy density and the cohesive energy). Thus, the short-side and long-side lattice constants, \(a\) and \(b\), were selected as important, dominant factors at the first stage of the material-design technology shown in Fig. 1.

At the second stage of Fig. 1, the author described the adhesive fracture energy as a function by interpolating the nine data in Table 4 with the Kriging method. The obtained function is shown in Fig. 7. The ideally most appropriate values of the important factors (the short-side and long-side lattice constants, \(a\) and \(b\)) are obtained as \(a = 0.338\) nm and \(b = 0.542\) nm, respectively. These values correspond to the L9 orthogonal array (Table 3) are shown in Fig. 7.

### Table 4 Calculated adhesive fracture energy.

| Ceramics 1/ Ceramics 2/ Ceramics 3 | 1st parameter: \(a\) | 2nd parameter: \(b\) | 3rd parameter: \(S\) | 4th parameter: \(C\) | Adhesive fracture energy \(D\) (mJ/m²) |
|------------------------------------|------------------|------------------|------------------|------------------|----------------------------------|
| VO/MgO/CaO                        | Level 1          | Level 1          | Level 1          | Level 1          | 0.112                            |
| VO/NiO/BeO                        | Level 1          | Level 2          | Level 2          | Level 2          | 0.122                            |
| VO/ZnO/TiO                       | Level 1          | Level 3          | Level 3          | Level 3          | 0.102                            |
| SrO/NiO/MnO                      | Level 2          | Level 1          | Level 2          | Level 2          | 0.129                            |
| SrO/CoO/CoO                      | Level 2          | Level 2          | Level 3          | Level 3          | 0.166                            |
| SrO/BaO/SrO                      | Level 2          | Level 3          | Level 3          | Level 3          | 0.119                            |
| K$_2$O/ZrO/ScO                   | Level 3          | Level 1          | Level 3          | Level 2          | 0.0941                           |
| K$_2$O/RbO/BeO                   | Level 3          | Level 2          | Level 1          | Level 3          | 0.0878                           |

Fig. 6 Results of sensitivity base on the orthogonal array.
By using an inhouse database of molecular dynamics. As a result, three-layer ceramics (CaO/ NiOMgO) was found to have the most appropriate values of material factors close to the RNA molecules. The authors found another simple ceramics for easier mass production by using an inhouse database of molecular dynamics. As a result, the authors selected two ceramic materials (CaO-5%MgO and ZrO2-37%MgO) that also have the same lattice constants as those of RNA. By calculating the adhesive fracture energy defined in Section 2.2, the values for the CaO-5%MgO and ZrO2-37%MgO were obtained as 0.186 J/m² and 0.185 J/m², respectively. These values are higher than any value shown in Table 4.

To clarify the reason that CaO-5%MgO and ZrO2-37%MgO have strong adhesion to RNA, the author visualized the atomic configuration of the coherent interface between the RNA and CaO-5%MgO, as shown in Fig. 8. Because Fig. 8 shows that negatively charged oxygen atoms of RNA can be seen through at the centers of the six-membered rings of the top ceramic layer (CaO-5%MgO) and that the configuration of the oxygen atoms are in harmony with the six-membered rings, the accumulation of atomic interactions caused by this harmony is considered to lead to the strong adhesion. The atomic configurations at the interfaces of RNA/ZrO2-37%MgO were found to be almost the same as that at RNA/CaO-5%MgO interface although the figures are not shown in this paper.

Although the figure is not shown, the atomic configuration of the interface between RNA and HfO2-28%MgO, whose lattice constants [a =0.339 nm and b=0.587 nm] are close to the optimal values, is similar to that in Fig. 8. The adhesion strength of the RNA/HfO2-28%MgO is fairly strong (0.184 J/m²). The film made of ceramic material (CaO-0.5%HfO2, CaO-0.5%Al2O3) has similar adhesion with RNA to HfO2-28%MgO although figures are not shown.

The atomic configurations of the interface between RNA and VO/ZnO/TiO2, whose lattice constants [a =0.287 nm and b=0.788 nm] are not close to the optimal values, are shown in Fig. 9. This figure shows that the configuration of RNA is disordered and that most of negatively charge...
oxygen atoms of RNA can not be seen through the six-membered rings centers of the top ceramic layer (VO).

Accordingly, negatively charged oxygen atoms of RNA are not positioned at energetically stable sites in Fig. 9 in spite of high surface energy and high cohesive energy. So, the accumulation of atomic interaction at the incoherent interface between the RNA and VO/ZnO/TiO₂ is smaller than that at the interface shown in Fig. 8. This is the reason that the adhesive fracture energy (0.102 J/m²) is much smaller than that of RNA/CaO-5%MgO (0.186 J/m²).

As shown in Fig. 10, a semi-coherent interface was obtained by using silica (SiO₂) whose lattice constants [a =0.306 nm and b=0.538 nm] are closer to the optimal values than those of VO/ZnO/TiO₂ and are more different from the optimal values than those of CaO-5%MgO. Figure 10 shows that most of negatively charged oxygen atoms of RNA can be seen through the six-membered rings of the top ceramic layer (SiO₂), although they are not seen through at the centers of the six-membered rings but near the edges of the rings. As shown in this figure, the shape of RNA on SiO₂ is a stable helix-like structure similar to that of RNA on CaO-5%MgO (Fig. 9). Accordingly, the interface between RNA and SiO₂ is more coherent than that between RNA and VO/ZnO/TiO₂ shown in Fig. 10. This is the reason that the adhesion strength of RNA/SiO₂ (0.144 J/m²) is higher than that of RNA/VO/ZnO/TiO₂ (0.102 J/m²). Thus, the accumulation of atomic interactions caused by the lattice matching at the interfaces between RNA and ceramics was found to be the most dominant factor in adhesion strength.

Although the adhesion of double-chain (double-stranded) DNAs whose stable structure is double helix are a little different from that of single-chain (single-stranded) RNAs, the adhesion of single-chain DNAs is similar to that of single-chain RNAs. Only by changing the hydroxyl (OH) groups to hydrogens (Hs) in sugar parts and changing uracil to thymine in RNAs, all of RNA simulation models were changed to single-chain DNAs. By using these models, CaO-5%MgO, ZrO₂-37%MgO, and HfO₂-28%MgO were found to have strong adhesion to single-chain DNAs as well as to RNAs because of similar single-chain structures. So, these ceramic materials can be used to attach single-chain DNA probes for detecting diseases[12].

By applying the same procedure to the design of ceramics with strong adhesion to peptides that are small parts of proteins, CaO-9%NiO whose lattice constants were equal to the best values (a =0.336 nm and b=0.582 nm), which are the lattice constants of beta-strand peptides, was selected. As shown in the coherent interface between CaO-9%NiO and the peptide (Fig. 11), the lattice matching leads to the largest adhesive fracture energy (0.184 J/m²). Simulations also showed that ZrO₂-34%NiO and HfO₂-26%NiO have strong adhesion to the peptide (0.182 J/m² and 0.181 J/m²) for the same reason (lattice matching). So, these ceramic materials can be used to absorb virus whose surface is made of peptide.

4 Comparison between Simulations and Experiments

To confirm the effectiveness of the molecular dynamics simulation technique described in Chapters 2 and 3, the author conducted a scratch test on the film-laminated structure (scratch tester: made by Rhesca Co., Ltd.) and compared the test results with the simulation results. Recently, more advanced methods for measuring adhesion strength have been proposed in a number of research papers[13]. However, these advanced methods were very difficult to apply to fairly strong interfaces such as the interface between RNA and CaO-5%MgO. Accordingly, a simple scratch-testing method that was applicable to the strong RNA/CaO-5%MgO interface was employed. In the scratch testing, a diamond indentor with a tip radius of 5 μm makes the dynamic indentations. During the measurement, load is gradually increased and when it reaches a critical load, adhesive fracture occurs at the interface. The adhesion strength is determined by measuring the critical load, L, at which the adhesive fracture occurs.

The author used RNAs attached on the ceramics for the scratch test. The test samples were prepared by using the same method as that shown in Ref. 3). First, the RNA/lipid complex obtained from yeasts was dissolved in the chloroform solution. The test samples were obtained by casting the chloroform solution (40 mg/mL) of the RNA/lipid complex on ceramic films sputter-deposited on silicon substrates under slow evaporation of the solvent at room temperature. For the ceramics, the author used the five ceramic multilayers (CaO-5%MgO, SiO₂, VO/MgO/CoO, SrO/NO/MnO₃, and K₂O/NO/MnO₃), three of which are listed in Table 4. These ceramic films were deposited on silicon substrates by using physical vapor deposition (PVD), and the thickness of each film was set at the same as that used in the simulations by controlling the deposition time. By using the 0-2θ scheme of the X-ray diffraction (XRD), the author selected the specimens that have significant diffraction peaks, which show single-orientation films.
The adhesive fracture energy, $D$, obtained from molecular simulations and the critical load, $L$, obtained from the scratch test of the interfaces between RNA films and ceramic multilayers are compared in Fig. 12. The ordered molecular orientation of RNA is considered to be one of the reasons for the small deviation and the good agreement between the simulations and experiments. Because the linear relationship can be seen between simulations and experiments, the adhesion-calculation method is found to be effective for determining the adhesion strength. Furthermore, from the results shown in Fig. 12, it is experimentally confirmed that the CaO-5%MgO multilayer, which was selected by using our material-design technology (Fig. 1), has the strongest adhesion to RNA. Thus, our technology for designing appropriate materials with a combination of an orthogonal array and a response-surface method is considered to be effective for designing a ceramic material that has strong adhesion to RNA.

5 Summary

A materials-informatics technology for efficiently designing a ceramic material with strong adhesion to organic materials with a combination of an orthogonal array and a response-surface method was used to design best ceramics with strong adhesion to single-chain RNAs and peptides. In this technique, at the first stage, important factors that significantly influence the adhesion strength were selected from various factors that characterize ceramics by use of an orthogonal array with molecular simulations. At the second stage, the adhesion strength was described as a function of the selected important factors by using a response-surface method. From this function, the best values of the important factors that made the adhesion strength maximum were obtained. At the third stage, the best ceramic materials whose important factors were close to the best values were selected. By carrying out these procedures on RNA/ceramics and peptide/ceramics, the following results were obtained.

(1) By using the sensitivity analysis based on an orthogonal array, the short-side and long-side lattice constants, $a$ and $b$, were selected as the important, dominant factors from four ceramic-multilayer factors (the lattice constants, $a$, $b$, the surface energy density, $S$, and the cohesive energy, $C$).

(2) By describing the adhesive fracture energy as a function of the important factors (the short-side and long-side lattice constants, $a$ and $b$), the best values for $a$ and $b$ that made the adhesion strength maximum were obtained as 0.338 nm and 0.585 nm, respectively. This result shows that lattice matching is important in the adhesion strength because the best values are equal to the lattice constants of RNA.

(3) Three multilayers (CaO-5%MgO ZrO$_2$-37%MgO, and HfO$_2$-28%MgO), whose lattice constants were $a=0.338$ nm and $b=0.585$ nm (the best values), were selected as the best ceramics with the strongest adhesion to RNA. These simulation results were confirmed by scratch testing.

(4) CaO-9%NiO, ZrO$_2$-34%NiO, and HfO$_2$-26%NiO were found to have strong adhesion to a peptide because of fair good lattice matching with the peptide.

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