

# Biocompatible Co-organic Composite Thin Film Deposited by VHF Plasma-Enhanced Atomic Layer Deposition at a Low Temperature

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Cite This: *ACS Omega* 2024, 9, 33735–33742



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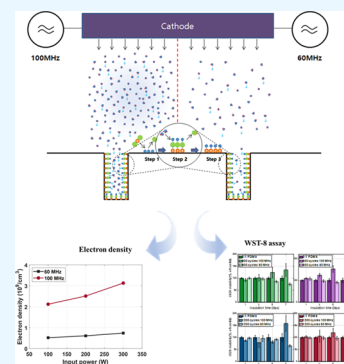
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**ABSTRACT:** Although metal–organic thin films are required for many biorelated applications, traditional deposition methods have proven challenging in preparing these composite materials. Here, a Co-organic composite thin film was prepared by plasma-enhanced atomic layer deposition (PEALD) with cobaltocene (Co(Cp)<sub>2</sub>) on polydimethylsiloxane (PDMS), using two very high frequency (VHF) NH<sub>3</sub> plasmas (60 and 100 MHz), for use as a tissue culture scaffold. VHF PEALD was employed to reduce the temperature and control the thickness and composition. In the result of the VHF PEALD process, the Young's modulus of the Co-organic composite thin film ranged from 82.0 ± 28.6 to 166.0 ± 15.2 MPa, which is similar to the Young's modulus of soft tissues. In addition, the deposited Co ion on the Co-organic composite thin film was released into the cell culture media under a nontoxic level for the biological environment. The proliferation of both L929, the mouse fibroblast cell line, and C2C12, the mouse myoblast cell line, increased to 164.9 ± 23.4% during 7 days of incubation. Here, this novel bioactive Co-organic composite thin film on an elastic PDMS substrate enhanced the proliferation of L929 and C2C12 cell lines, thereby expanding the application range of VHF PEALD in biological fields.



## INTRODUCTION

Metal ions play fundamental roles in biology by serving as essential elements in various processes, such as respiration, growth, gene transcription, enzymatic reactions, cell proliferation, and immune function.<sup>1</sup> Most metal ions combine with proteins in the body to produce metalloproteins, which are some of the most efficient inorganic catalysts, catalyzing important biological reactions, such as photosynthesis, respiration, water oxidation, signal transduction, and complex chemical transformations.<sup>2</sup> However, these essential metals can be toxic at high concentration levels; therefore, the metabolism and secretion of metal ions must be tightly regulated at cellular levels. Generally, metal ions, including Ca<sup>2+</sup>, Co<sup>2+</sup>, Cu<sup>2+</sup>, Mg<sup>2+</sup>, Mn<sup>2+</sup>, Na<sup>+</sup>, Ni<sup>2+</sup>, and Zn<sup>2+</sup>, are essential nutrients for supporting microorganisms and are required as trace elements at nanoscale molar concentrations.<sup>3–5</sup> They stabilize protein structures and cell walls and osmotic balance pressure.<sup>6,7</sup> Especially, Co<sup>2+</sup>, a crucial trace element, is vital for human health. Its organic form, found in vitamin B12, plays a key role in nerve cell function and neurotransmitter production. Therefore, it is important to keep the concentration of metal ions at appropriate levels to maintain human health. This understanding highlights the potential *in vivo* applications of metal–organic thin films.

Designing materials at nanometer-scale dimensions on organic substrates is crucial for advancements in various fields, such as scaffolding, tissue engineering, drug delivery, and smart polymer engineering. The primary methods that researchers

employ to achieve this include self-assembled monolayers and engineered supermolecular interactions. However, depositing metals at nanometer-scale dimensions on organic substrates in a controlled manner has proven challenging using conventional deposition techniques. The sol–gel method, often used to deposit metals on organic thin films, is favored for its simplicity and ease with which it allows control of chemical elements. Nevertheless, it presents its own set of challenges, particularly in adjusting the thickness of thin films. Additionally, this process necessitates a secondary heating stage to eliminate byproducts.<sup>8–12</sup> Cold plasma deposition offers an alternative, relatively straightforward process, enabling the conversion of organometallic compounds into metal–organic composite thin films. Despite its potential, progress in this method has been limited. This is primarily due to the high cost and scarcity of volatile and stable organometallic compounds.<sup>13–20</sup> Notably, cold plasma deposition allows for the precise deposition of nanometer-scale metal–organic compounds on organic biocompatible substrates.

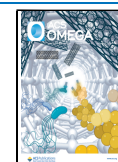
Polydimethylsiloxane (PDMS), a nontoxic organic material approved by the US Food and Drug Administration, is

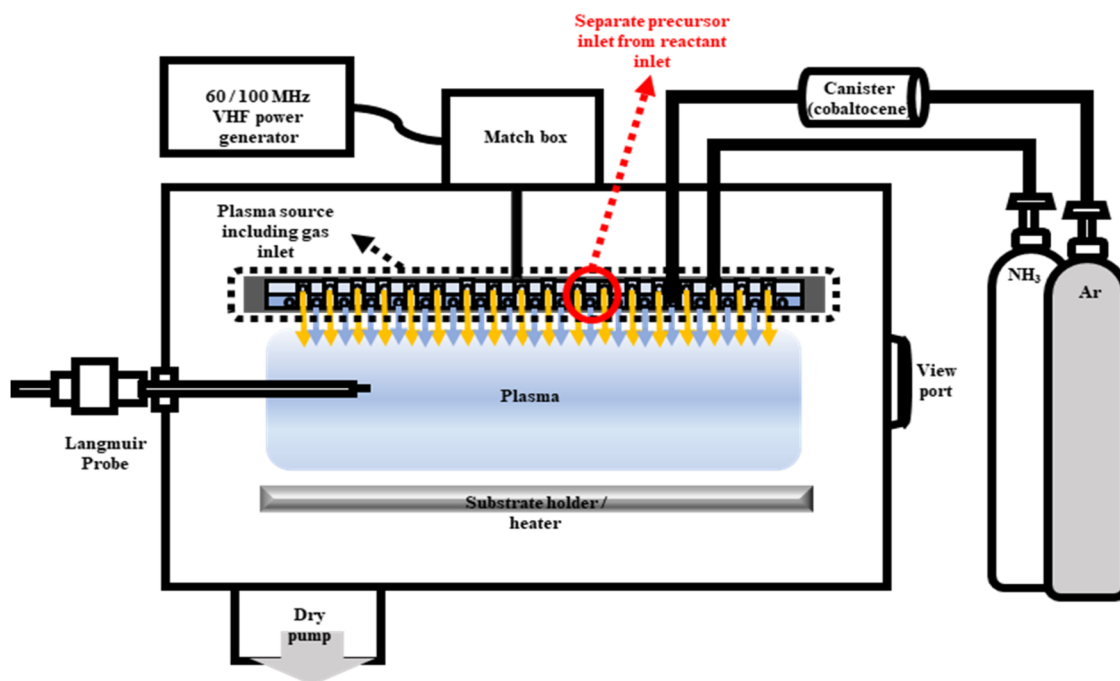
**Received:** March 25, 2024

**Revised:** May 24, 2024

**Accepted:** May 27, 2024

**Published:** July 23, 2024





**Figure 1.** Schematic drawing of the capacitively coupled plasma (CCP)-type plasma-enhanced atomic layer deposition (PEALD) system.

extensively used in medical applications.<sup>21–23</sup> The chemical and physiological stability of PDMS makes it an ideal material for long-term body implants, including cardiac pacemakers, mammary implants, maxillofacial, voice, and finger joint prostheses, drainage tubes, and catheters. Consequently, the development of a Co-organic composite thin film on PDMS is anticipated to enhance the biocompatibility synergistically.

In this study, we successfully fabricated a Co-organic composite thin film using very high frequency plasma-enhanced atomic layer deposition (VHF PEALD) at a low temperature.<sup>24,25</sup> The Co-organic composite thin film was effectively deposited on PDMS using VHF (60 and 100 MHz) by PEALD over 900 and 1200 cycles at a low temperature of 100 °C. We also investigated the cytotoxicity of the Co-organic composite thin film.<sup>26</sup> The Co-organic composite thin film, deposited at 100 MHz after 1200 cycles, demonstrated nontoxic properties, with a high C2C12 cell growth rate of  $164.9 \pm 23.4\%$  observed after 7 days of incubation.<sup>26</sup> X-ray photoelectron spectroscopy (XPS) results indicated that the Co-organic composite thin film deposited using a VHF of 100 MHz had an increased Co percentage and decreased O and C percentages compared with that deposited at 60 MHz. This composition facilitates the release of Co ions into the solution. Therefore, we anticipate that the Co-organic thin film deposited using VHF by PEALD can enhance the biocompatibility of a metal–organic composite thin film.<sup>27</sup>

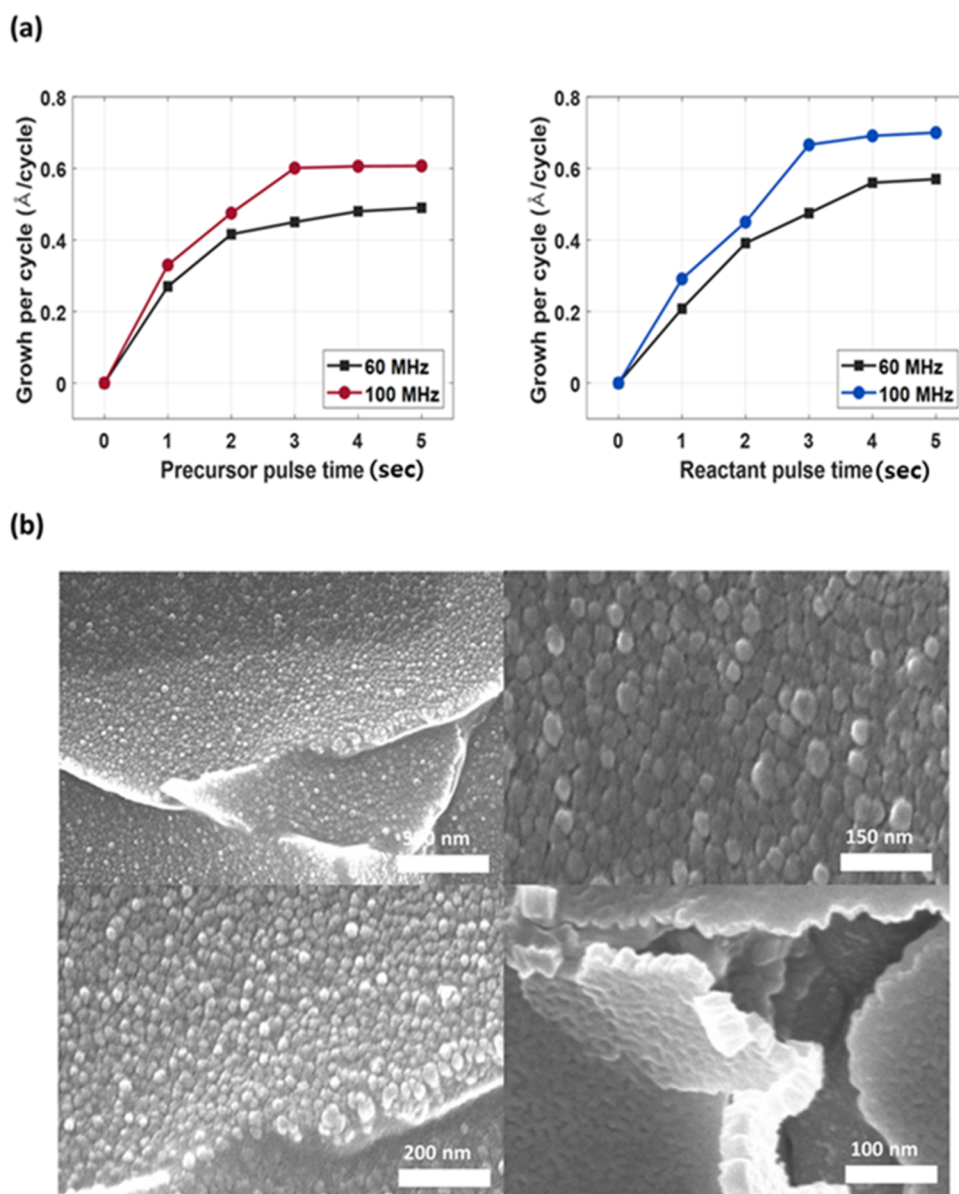
## EXPERIMENTAL DETAILS

**Figure 1** presents a schematic representation of the capacitive coupled plasma (CCP)-type PEALD system utilized in our experiment. The chamber, constructed from anodized Al, measures 450 mm × 450 mm with a height of 300 mm. A VHF power was applied to the top electrode, with the substrate positioned on the bottom-facing electrode. To deliver the VHF power, 60 and 100 MHz radio frequency powers were alternately connected to the top electrode via a corresponding matching network. The precursor and reactant gases were

uniformly distributed from the shower head located on the top power electrode. The gas holes for the precursor and reactant gases were separated to prevent cross-contamination. A precursor canister, a 250 cc glass bottle, was positioned close to the processing chamber, allowing for easy monitoring of the precursor flow and the remaining amount. The canister and connecting tube were heated to ensure efficient delivery of the precursor to the processing chamber during the PEALD.

Under these process conditions, we anticipated additional conversion of potential energy to thermal energy using the VHF plasma at a relatively low temperature of 100 °C, given the low heat resistance of PDMS, which necessitates careful temperature control to prevent thermal degradation during deposition. Cobaltocene ( $\text{Co}(\text{Cp})_2$ ), a solid source, was used as the precursor for Co, with  $\text{NH}_3$  serving as the reactant gas. To economize on the Co precursor, we chose  $\text{Co}(\text{Cp})_2$  due to its sufficient volatility and stability.<sup>28–32</sup> Argon (Ar) was used as both a carrier gas for the precursor and a purging gas during each step. To deposit the Co-organic composite thin film on the PDMS substrate, we used a low substrate temperature of 100 °C, with both the gas line and canister heated at 90 °C. This approach differs from previous studies, where deposition occurred at a high temperature of 300 °C.<sup>33</sup> We flowed 200 mTorr  $\text{Co}(\text{Cp})_2$  to the substrate for 0–5 s for precursor adsorption. To maintain a constant pressure of 200 mTorr, we flowed a mixed gas (150 sccm), comprising a  $\text{CoCp}_2$  precursor and Ar carrier gas, necessitating the measurement of total pressure due to the  $\text{CoCp}_2$  solid source. Subsequently, 200 mTorr  $\text{NH}_3$  was flowed for 0–5 s with a VHF plasma power of 200 W for the reaction, following a 3 s reactant gas stabilization step with  $\text{NH}_3$ . After each step, the gases were purged/evacuated for 25 s.

For characterization, we used a cutoff probe (SALUKI, S3601B) to measure the plasma characteristics of the VHF plasma, such as electron density. We measured the degree of  $\text{NH}_3$  gas dissociation during the operation of the VHF plasma using optical emission spectroscopy (OES, AvaSpec-3648,



**Figure 2.** Growth per cycle (GPC) measured as a function of (a)  $\text{Co}(\text{Cp})_2$  exposure time (with 5 s of  $\text{NH}_3$  exposure time) and  $\text{NH}_3$  exposure time (with 5 s of  $\text{Co}(\text{Cp})_2$  exposure time) for 60 and 100 MHz VHF  $\text{NH}_3$  plasmas. 200 mTorr  $\text{Co}(\text{Cp})_2$  and  $\text{NH}_3$  were used during the precursor and reactant exposure steps, respectively. (b) Scanning electron microscopy (SEM) images of the Co surface deposited by capacitively coupled plasma (CCP)-type plasma-enhanced atomic layer deposition (PEALD) for 1200 cycles with 100 MHz on the polydimethylsiloxane (PDMS) substrate.

Avantes). We observed the surface morphology and thickness using a field-emission scanning electron microscope (FESEM, Hitachi S-4700, Hitachi), and the composition percentage of the deposited Co thin films was observed by X-ray photoelectron spectroscopy (XPS, Multilab 2000, Thermo VG, Mg  $K\alpha$  source). As for PDMS used in the experiment, a Sylgard 184 silicone elastomer kit was purchased from Sigma-Aldrich. The silicone elastomer base and curing agent were mixed in a volume ratio of 10:1 in a beaker. We continuously stirred with a glass rod for 7 min in a beaker on behalf of the homogeneous mixture. In order to remove the bubble from the mixer, the mixture was placed in a vacuum drier for 30 min. After degassing, these PDMS substrates were cured in an oven at 100 °C. We measured the Young's modulus, reduced modulus, and hardness of the bare PDMS and Co-organic composite thin film samples using a nanoindenter (NanoTest Vantage Platform) with a Poisson's ratio of 0.50 and a maximum load of

0.01 mN. We used inductively coupled plasma-optical emission spectroscopy (ICP-OES, Varian) to quantify the released Co ions from the Co-organic composite thin film according to the Korean Industrial Standards M 0025-2008.<sup>33</sup> We conducted the WST-8 assay (Viability Assay Kit, B1007, Cellrix), according to the manufacturer's instructions, to calculate the long-term *in vitro* cytotoxicity. We selected L929 cells for the *in vitro* cytotoxicity assay in accordance with ISO 10993-5, while C2C12 cells were chosen due to the elasticity of the Co-organic composite thin film on the elastic PDMS substrate that released Co ions into the biological environment. C2C12 cells were known to proliferate in a biological environment with elastic properties, which aligned with the physicochemical conditions of this study. For the WST-8 assay, we selected the control PDMS group based on the measured Young's modulus in this study.

## RESULTS AND DISCUSSION

Figure 2a illustrates the growth behavior of the Co thin film on PDMS using PEALD under the specified VHF plasma

**Table 1. Atomic Percentages of a Co-organic Composite Thin Film on Polydimethylsiloxane (PDMS)**

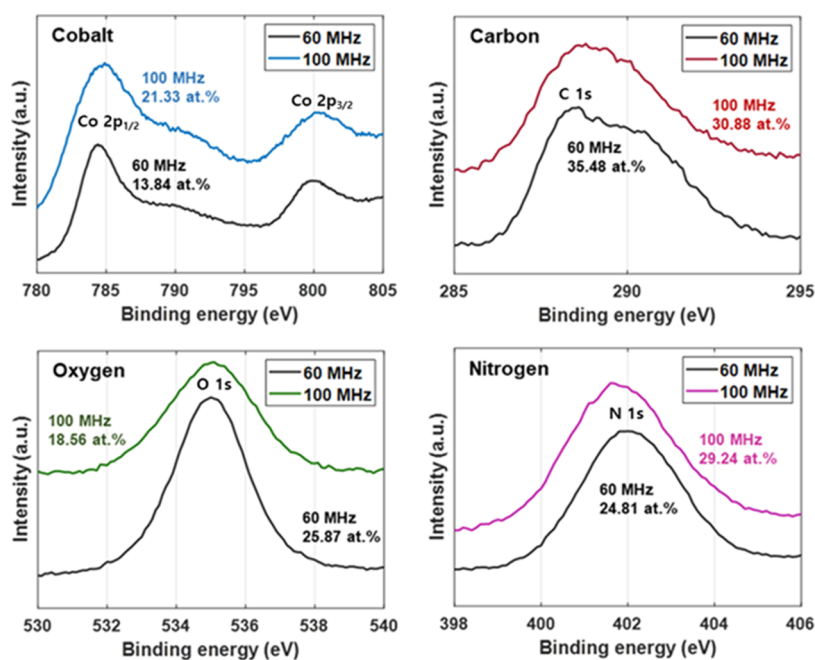
	Co 2p (%)	C 1s (%)	O 1s (%)	N 1s (%)
100 MHz	21.33	30.88	18.56	29.24
60 MHz	13.84	35.48	25.87	24.81

conditions as a function of precursor adsorption time and  $\text{NH}_3$  plasma reaction time. An increase in precursor and  $\text{NH}_3$  plasma exposure times resulted in an increase in the growth per cycle (GPC, Å/cycle) until the precursor and  $\text{NH}_3$  plasma exposure times of approximately 3 and 4 s, respectively, were reached. Any further increase in the precursor and  $\text{NH}_3$  plasma exposure times during the adsorption and reaction steps saturated the GPC up to an exposure time of 5 s. The provided duration can be determined through an assessment of the saturation point. Interestingly, while the time required for saturation during the precursor adsorption and  $\text{NH}_3$  plasma reaction steps was the same for both 60 and 100 MHz, the GPC was higher for 100 MHz compared to 60 MHz. This outcome could be attributed to the highly dissociated  $\text{NH}$  radicals in the plasma during the reaction step, as indicated in a previous study.<sup>24</sup> Figure 2b presents SEM images of the Co-organic composite thin film deposited by the VHF CCP-type PEALD after 1200 cycles at 100 MHz. The Co film deposited at the VHF displayed a polycrystalline structure with typical porosity at a low temperature and limited diffusion. We obtained side images (SEM) of the Co-organic composite thin films by flash-freezing PDMS in liquid nitrogen, which demonstrated flexibility. The adhesion between the PDMS polymer and the Co metal was confirmed. In a previous study,

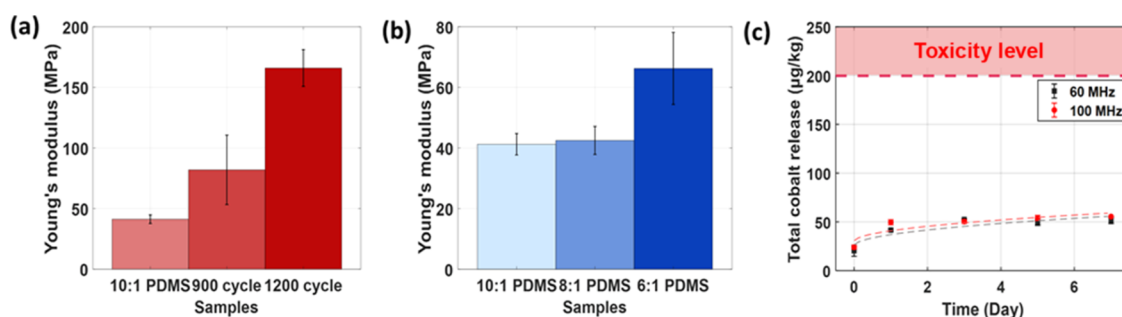
Co thin films deposited at 100 MHz were observed to be smoother than those at 60 MHz, underscoring the necessity of a VHF to activate the reactant gas.<sup>24</sup>

The composition of the Co-organic composite thin film was analyzed using XPS, with the results presented in Table 1 and Figure 3. The atomic percentages presented in Table 1 and shown in Figure 3 were obtained from the survey spectra analyzed by X-ray photoelectron spectroscopy (XPS). We utilized the data from the survey spectra to calculate the composition of the Co-organic composite thin film. The deposited Co ( $2p_{1/2}$ ,  $2p_{3/2}$ ) thin film contained additional components, including C 1s, N 1s, and O 1s. The percentages of C and O were notably high, approximately 35.5 and 26%, respectively, while the Co percentage in the film deposited by PEALD was around 22%. The presence of N in the film is attributed to the use of  $\text{NH}_3$  plasma. When a VHF of 100 MHz was used, as opposed to 60 MHz, the composition percentages of Co increased, while the proportions of O and C percentages decreased. As depicted in Figure 3, the purity of Co increased more at a higher frequency. It is postulated that the presence of other components, such as carbon, oxygen, and nitrogen, in addition to Co in the film during the PEALD process, is partially due to the low deposition temperature of 100 °C and the use of  $\text{NH}_3$  plasma.

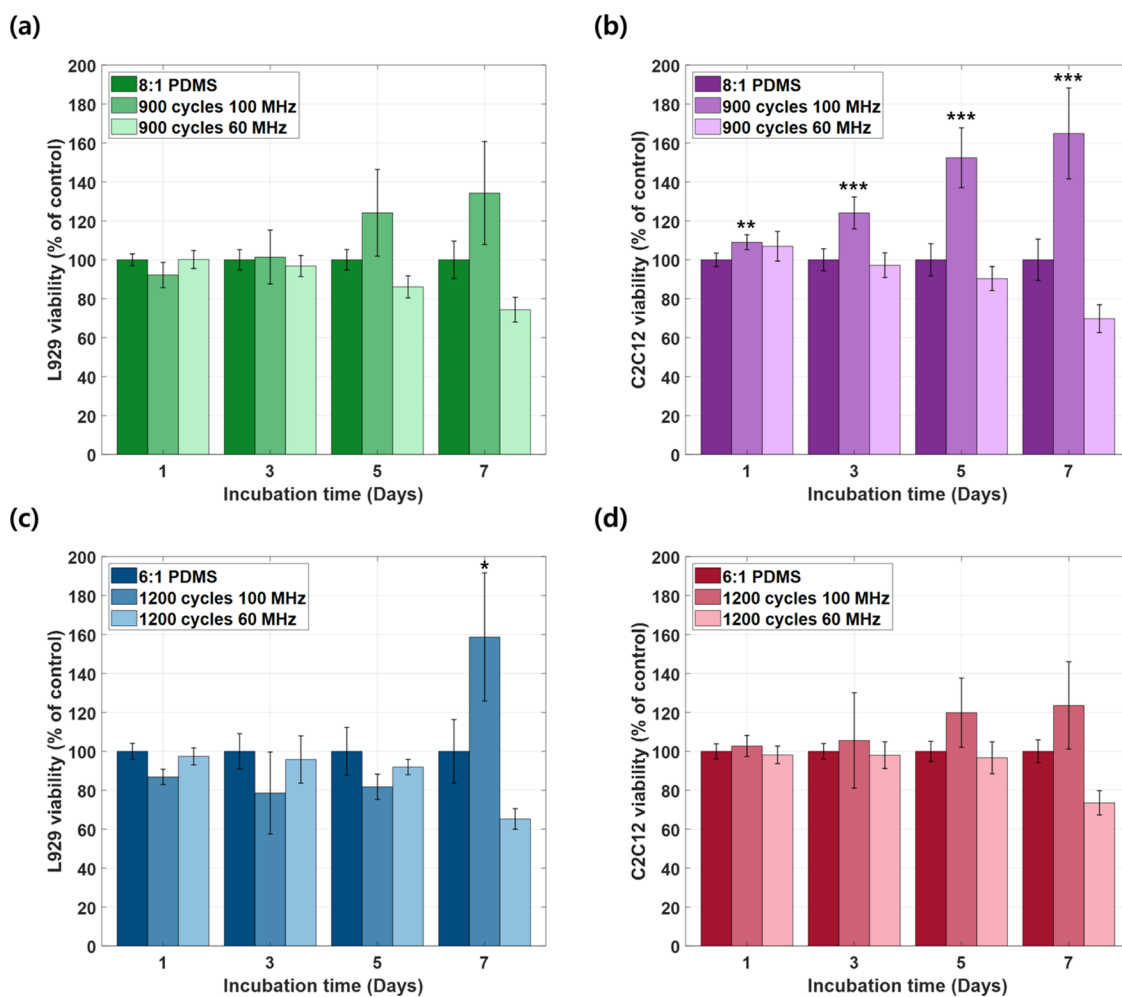
The interaction between cells and the extracellular matrix significantly influences various cellular behaviors, such as growth, proliferation, and differentiation. Similarly, the mechanical properties of the material interacting with a cell are of great importance.<sup>34–38</sup> Therefore, we characterized the mechanical properties of the Co-organic composite thin film deposited on PDMS, prepared in different ratios between the silicone elastomer base and the curing agent, using nano-indentation to determine whether any significant changes could be induced in the Co-organic composite thin film. 10:1 PDMS was initially chosen to study the influence of VHF



**Figure 3.** Narrow-scan X-ray photoelectron spectroscopy (XPS) results of the Co-organic thin films deposited by capacitively coupled plasma (CCP)-type plasma-enhanced atomic layer deposition (PEALD) at 60 and 100 MHz. Spectra of Co, C, N, and O are shown. For the adsorption and reaction steps, 5 s and 200 mTorr of the  $\text{Co}(\text{Cp})_2$  precursor and  $\text{NH}_3$  plasma were used, respectively.



**Figure 4.** Young's modulus results and Co-ion release kinetics analyzed through ICP-OES. (a) 100 MHz VHF PEALD was applied on 10:1 polydimethylsiloxane (PDMS) for 900 cycles and 1200 cycles. The Young's modulus of the samples was measured by nanoindentation. (b) The mixing ratio of the elastomer and curing agent was controlled to adjust the Young's modulus of the PDMS substrate. The Young's modulus of the adjusted PDMS was investigated to establish the control group for the VHF PEALD samples. (c) The long-term Co ion release kinetics into the 1X phosphate buffer solution (PBS) were investigated in the 900-cycled film on the 10:1 PDMS by ICP-OES.



**Figure 5.** WST-8 assay confirmed the biocompatibility of (a) L929 after 900 cycles, (b) C2C12 after 900 cycles, (c) L929 after 1200 cycles, and (d) C2C12 after 1200 cycles. All data were presented as a ratio (%) based on each bare polydimethylsiloxane (PDMS) control group. All statistical analysis results were compared to those of the control group. Note: (\*) for  $P < 0.005$ , (\*\*) for  $P < 0.0005$ , and (\*\*\*) for  $P < 0.0001$  ( $n = 8$ ).

PEALD cycles, as it could potentially lead to issues, such as PDMS cracking or thin film detachment from the substrate. The results confirmed the successful deposition of the thin film on the 10:1 PDMS. The Young's modulus of the 10:1 PDMS substrate was measured to be  $41.3 \pm 3.5$  MPa, increasing to  $82.0 \pm 28.6$  and  $166.0 \pm 15.2$  MPa after 900 and 1200 cycles of deposition using 100 MHz VHF PEALD, respectively, with thicknesses of 567 and 756 Å in GPC 0.63 Å/cycle, as shown

in Figure 4a. To further vary the Young's modulus of the Co-organic composite thin film, we applied a 200 W energy VHF PEALD cycle to the PDMS substrate. However, when the mixing ratio was decreased to less than the 6:1 ratio, the PDMS substrate developed several cracks during curing. The Young's modulus was measured to be  $42.5 \pm 4.6$  and  $66.3 \pm 11.9$  MPa at the PDMS mixing ratios of 8:1 and 6:1, respectively, as shown in Figure 4b. Notably, this difference in

Young's modulus due to the curing agent ratio was significantly lower than the difference observed with increasing VHF PEALD cycles. Co ions play many key roles in human body metabolism, including vitamin B12 absorption, hemoglobin formation, treatment of anemia, certain infectious diseases, and repair of myelin. However, Co ions of over 200  $\mu\text{g}/\text{kg}$  per day are reported to be toxic. We employed Inductively Coupled Plasma-Optical Emission Spectroscopy (ICP-OES) to analyze the Co ion release kinetics from the Co-organic composite thin film on the PDMS substrate into 1 $\times$  PBS during long-term incubation. The released Co ions were calculated to be  $55.5 \pm 0.6 \mu\text{g kg}^{-1}$  for 100 MHz and  $51.2 \pm 2.9 \mu\text{g kg}^{-1}$  for 60 MHz after 7 days of incubation, which are considerably lower than the toxic limit for the human body.

Given the beneficial effects of Co ions on the human body, as previously discussed, Co-organic composite thin films are anticipated to promote cell proliferation in a biological environment. To investigate the scaffold effect of these films, we performed a WST-8 assay with L929 (mouse fibroblast cells) and C2C12 (mouse myoblast cells) cultured on Co-organic composite thin films prepared at different VHF (Figure 5). The Co-organic composite thin film on the PDMS substrate at 100 MHz demonstrated that both L929 and C2C12 cells proliferated during incubation. The highest C2C12 proliferation rate was observed at  $164.9 \pm 23.4\%$  after 900 cycles in the 100 MHz sample after 7 days of incubation. In contrast, a decrease in the proliferation of L929 and C2C12 cells was observed in the 60 MHz sample after 900–1200 cycles. XPS analysis revealed a higher composition of Co atoms at 100 MHz compared to 60 MHz. This suggests that the high frequency leads to a lower potential drop in the sheath region, resulting in less damage to the polymer surface during deposition. As a result, the deposition of Co-organic composite thin films, which influence cell metabolism and environment, is facilitated. This is believed to have promoted the proliferation of L929 and C2C12 cells. While the Young's modulus and the presence of other atoms, such as C, N, and O, may have some influence, the primary driver of cell proliferation appears to be the presence of Co atoms in the composite thin film.

## CONCLUSIONS

In this study, we explored the impact of VHF (60 and 100 MHz) on the deposition of a Co thin film on an organic substrate and the biological properties of the resulting Co-organic composite thin film. By manipulating the VHF, we were able to tune the composition percentage of the Co-organic composite thin film, resulting in increased Co and decreased O and C at the VHF of 100 MHz at approximately 100 °C. We also found that we could control the Young's modulus of the Co-organic composite thin film. Our findings indicate that the Co-organic composite thin film is biocompatible. The amount of Co released from the surface was significantly below the cytotoxicity level, and we observed an enhanced proliferation of mouse fibroblast and myoblast cell lines. This study reports the successful fabrication of a biocompatible metal-organic composite thin film using VHF PEALD at a low temperature. This method holds promise for various biological and biomedical applications.

## ASSOCIATED CONTENT

### Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/acsomega.4c02845>.

Process steps for the plasma-enhanced atomic layer deposition (PEALD) cycle used in the experiment, electron density as a function of very high frequency (VHF) power for the frequencies of 60 and 100 MHz with a capacitively coupled plasma (CCP)-type plasma source and 200 mTorr  $\text{NH}_3$ , average modulus and hardness of bare, 900-cycle, and 1200-cycle films deposited by plasma-enhanced atomic layer deposition (PEALD) with Co and  $\text{NH}_3$  on polydimethylsiloxane (PDMS), and experimental detail (PDF)

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### Author Contributions

#W.K.Y. and J.W.L. contributed equally to this work.

### Notes

The authors declare no competing financial interest.

## ACKNOWLEDGMENTS

This research was supported by the Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education (NRF-2019R1A6A1A03033215) and by the Korea Basic Science Institute (KBSI) National Research Facilities & Equipment Center (NFEC) grant funded by the Korean government (Ministry of Education) (No. 2019R1A6C1010031)

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