Application of Plackett-Burman and Box-Behnken experimental designs in differential voltammetry for determining Gadolinium concentration

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Abstract. Middle group rare earth elements, such as Gadolinium, have an important role in a variety of applications, mostly used in high-tech industries because they have good mechanical strength. However, the rare earth elements of this middle group are difficult in their analysis because each element has almost the same physical and chemical properties. Gadolinium is one of the rare earth elements that have high paramagnetic properties. The purpose of this study was to determine the gadolinium content by differential pulse voltammetry using an experimental design. Plackett-Burman experimental design was used to obtain selected factors that have positive results to the method. A total of 11 factors that have the potential as the main influence in this study were selected at the highest (+) and lowest (-) levels, and then measured 12 times according to the Plackett-Burman experimental design. Furthermore, optimization was carried out with the Box-Behnken experimental design by performing 15 measurements to obtain the optimum conditions for each factor. Response data was processed and obtained factors with optimum conditions, deposition potential of -2.0 V, modulation of the amplitude of 0.1 V, and a deposition time of 120 seconds. The detection limit and the quantitation limit were 3.97 mg/L and 10.71 mg/L, respectively. The recovery of Gadolinium was 95%, which is satisfactory.

1. Introduction

Rare earth elements are 14 lanthanide elements with atomic numbers ranging from 57 (La) to 71 (Lu), which have similar chemical and physical properties as well as scandium and yttrium. Gadolinium is one of the rare earth elements that have paramagnetic properties and meets important requirements as a contrasting agent [1]. The two most commonly used methods for analyzing REEs are Inductive Plasma-Mass Spectrometry (ICP-MS) and Instructional Neutron Activation Analysis (INAA). While INAA has the advantage because the time for analysis is longer and the detection limit is higher than ICP-MS [2]. However, these instruments have drawbacks such that sample preparation takes a long time and the measurement conditions cannot be adjusted so that it cannot be optimized. Meanwhile, electrochemical techniques have advantages in sensitivity, probability and relatively low cost [3,4].

Differential pulse voltammetry is an analytical method that is a method of measuring the current response of an analyte by applying a potential to the electrode. The resulting current response comes from electron transfer during the oxidation and reduction process of the analyte [5].
The voltammetry cell consists of a working electrode, a supporting electrode and a comparison electrode. The three electrodes were immersed in a voltammetry cell containing a sample solution. Outside potential is applied between the working electrode and the comparison electrode. If there is an oxidation or reduction reaction at the working electrode, the resulting current will be passed to the auxiliary electrode, so that the reaction that occurs at the auxiliary electrode will be opposite to the reaction that occurs at the working electrode [6].

Voltammetry has the advantage of being in the provision of simple samples that are fast analysis times and can reduce the source of errors with a detection limit of up to 0.1 µg/L [7].

Along with the rapid increase of science and technology now causes the research process to be more complicated, so we need a method that can investigate a large number of factors involved in research and determine what factors significantly influence the research. Experimental design methods can be applied to parameter selection that has a strong influence on research. The 2-level Plackett-Burman (PB) experimental design is a design that measures as much ask (s-1) +1, where k is a factor and s is a level. Research testing 11 factors only requires 12 measurements using the PB design, so it saves more time and costs compared to using a 2-level factorial design [8].

In this study, Gd rare earth elements were analyzed using the differential pulse voltammetry (DPV) method by conducting the Plackett-Burman experimental design for the determination of factors that had a significant impact on the analysis.

2. Methods
The materials used in this study include pure water (Milli-Q water), hydrochloric acid (HCl, Merck), nitric acid (HNO₃, Merck), citric acid (C₆H₈O₇·2H₂O, Merck), ammonium chloride (NH₄Cl, Merck) and sodium hydroxide (NaOH, Merck), gadolinium oxide (Gd₂O₃, Sigma Aldrich), sodium hydroxide (NaOH, Merck), sodium citrate (C₆H₅Na₃O₇·2H₂O, Merck). All solutions were diluted with pure water.

2.1. Analysis of Gd solution
Gd solutions (variations in concentrations of 10, 15, 20, 25 and 30 mg/L) of 10 mL were inserted in voltammetry cells and then measured using the VPD method with conditions of deposition time of 120 s, amplitude modulation of 0.1 V, scan rate of 0.05 V/s, and the potential range from -3.5 to +1.0 V.

2.2. Background of current measurement
A total of 10 mL of supporting electrolyte solution was placed in a voltammetry cell. The three electrodes were connected to the potentiostat then measurements were made using differential pulse voltammetry in the potential range of -3.5 V to +1 V, deposition potential of -3.5 V, deposition time of 120 seconds, and a scanning rate of 0.05 V/s.

2.3. Design of Plackett-Burman experiments
Gadolinium solutions were analyzed by the Plackett-Burman experimental design method for 12 measurements. Design of Plackett-Burman experiments with factors of using pretreatment or not, use of stirring or not, the pH of the solution in voltammetry cells with low and high levels, low and high level deposition potentials, low and high level step potentials, low and high level amplitude modulation, low and high level interval times, low and high level deposition times, low and high-level equilibrium times used.

2.4. Making the Box-Behnken experimental design
The selected factors from Plackett-Burman are then optimized using the Box-Behnken design. The analysis process using differential pulse voltammetry is the same as the analysis process in the Plackett-Burman design, which distinguishes namely the number of experiments and the level of factors performed.
2.5. Gadolinium current response measurement
As much as 3 mL of gadolinium solution was inserted into a voltammetry cell then 4 mL of pure water was added. The three electrodes were connected to the potentiostat and then measured using differential pulse voltammetry with optimum conditions from the Box-Behnken experimental design.

2.6. Preparation of standard curve
Gd concentration variation solution was put into a voltammetry cell as much as 3 mL then added 6 mL pure water. Then the three electrodes are connected to a potentiostat and a measurement of the use of differential pulse voltammetry with optimum conditions from the Box Behnken experimental design.

3. Results and discussion
3.1. Background flow response
Measurement of background current response aims to determine the effect of electrolyte solution on the peak generated during the Gd measurement. Based on the measurement results of the NH₄Cl electrolyte solution and aquamili-Q obtained a voltammogram shown in Figure 1. Based on the voltammogram it can be seen that during the measurement process the electrolyte solution of the aquamili-Q solution does not produce peak currents that can interfere with the measurement process of gadolinium metal. So it can be concluded that aquamili-Q can be used as a supporting electrolyte solution.

![Voltammogram](image)

**Figure 1.** Voltammogram (a) 0.1 M ammonium chloride (NH₄Cl) electrolyte solution and (b) aquamili-Q with a potential range of -3.5 to +1.0 V, deposition potential of -3.5 V, deposition time 120 s and a scan rate of 0.05 V/s.

3.2. The choice of factors influences the differential pulse voltammetry analysis
Voltammetry is a flow measurement analysis technique as a function of potential, the measured current is proportional to the concentration of the analyte according to the Randles-Sevcik equation [9]:

\[
ip = 0.4463 \, nFAC \, \sqrt{\frac{nFvD}{RT}}
\]

where \(ip\): peak current, \(n\): number of electrons, \(F\): Faraday's constant, \(T\): temperature, \(R\): gas constant, \(A\): surface area of the working electrode, \(D\): diffusion coefficient, \(v\): scan rate, and \(C\): concentration.

The surface area of the working electrode (A) is not optimized because it is fixed, pencil graphite is not modified. Faraday's constant (96485 C/mol), gas constant (8.314 J/Kmol) and temperature (25°C) are not changed so there is no need to be optimized.

The diffusion coefficient (D) is the transfer of matter or the movement of electrons from high to low concentrations. In voltammetry analysis, the analyte will stick to the surface of the working electrode...
then the oxidation-reduction reaction occurs, electrons are measured in the form of a current. Deposition of the analyte to the electrode can occur due to diffusion, migration (charge difference) and convection (stirring). For optimal reduction of the analyte on the electrode, it is necessary to optimize the supporting electrolytes used and stirring. Supporting electrolytes function to increase the conductivity of the solution, the electrolytes tested are strong electrolytes (NH$_4$Cl) and non-electrolytes (H$_2$O).

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$$E = E^0 - \frac{RT}{nF} \log \frac{1}{[C]}$$

where E: standard reduction potential, for optimal electron transfer, deposition potential and deposition time must be optimized. In the analysis of differential pulse voltammetry, the scan is carried out from negative potential to positive potential so optimization potential range is needed. Amplitude and scan rate pulses also need to be optimized, because they affect the resolution (separation) and measurement sensitivity. All factors are shown in Table 1.

### Table 1. Factors that might have a significant effect on Gd analysis in differential pulse voltammetry.

| Factor               | Low (-) | High (+) |
|----------------------|---------|----------|
| X1 Pretreatment      | No      | Yes      |
| X2 Stirring          | No      | Yes      |
| X3 pH                | 5       | 7.5      |
| X4 Deposition potential | -3.5 V | -2 V     |
| X5 End potential     | 1 V     | 2 V      |
| X6 Step potential    | 0.001 V | 0.025 V  |
| X7 Amplitude modulation | 0.05 V | 0.1 V   |
| X8 Interval time     | 0.1 s   | 0.5 s    |
| X9 Deposition time   | 60 s    | 180 s    |
| X10 Balance time     | 10 s    | 30 s     |
| X11 Dummy            | -       | -        |

Measurement of Gd was carried out 12 times running which produced a response in the form of a current that was entered into the Minitab 18 program shown in Table 2.

The data from the Plackett-Burman experimental design is then processed and obtained the coefficient of the response function using a linear equation where Y is the response, X is the factors that influence the response and β is the intercept shown in equation (1).

$$Y = 0.004179-0.001065X1 + 0.000681X2-0.000286X3 + 0.00973X4-0.000675X5 + 0.003096X6 + 0.01650X7-0.003665X8 + 0.000006X9-0.000012X10-0.000000X11$$

(1)
Based on equation 1, it can be determined the factors that have a positive influence on Gd analysis using the differential pulse voltammetry method, namely, X4 (deposition potential), X7 (amplitude modulation) and X9 (deposition time) used to determine the optimum conditions of gadolinium analysis.

**Table 2.** Response 12 times the Plackett-Burman measurement.

| Run | X1 | X2 | X3 | X4  | X5  | X6  | X7  | X8  | X9  | X10 | X11 | Response (10^6 A) |
|-----|----|----|----|-----|-----|-----|-----|-----|-----|-----|-----|------------------|
| 1   | T  | T  | 5  | -2  | 2   | 0.025 | 0.05 | 0.5 | 180 | 10  | -   | 1.3143          |
| 2   | T  | T  | 5  | -3.5 | 1  | 0.001 | 0.05  | 0.1 | 60  | 10  | -   | 3.2851          |
| 3   | T  | Y  | 7.5 | -2  | 1   | 0.025 | 0.1   | 0.1 | 180 | 10  | -   | 5.6512          |
| 4   | Y  | Y  | 5  | -2  | 1   | 0.001 | 0.05  | 0.5 | 180 | 30  | -   | 3.1531          |
| 5   | Y  | T  | 7.5 | -3.5 | 1  | 0.001 | 0.1   | 0.5 | 180 | 10  | -   | 1.3303          |
| 6   | Y  | Y  | 7.5 | -3.5 | 2  | 0.025 | 0.05  | 0.5 | 60  | 10  | -   | 3.1542          |
| 7   | T  | Y  | 5  | -3.5 | 1  | 0.025 | 0.1   | 0.5 | 60  | 30  | -   | 4.4312          |
| 8   | Y  | Y  | 5  | -2  | 2   | 0.001 | 0.1   | 0.1 | 60  | 10  | -   | 0               |
| 9   | T  | T  | 7.5 | -2  | 2   | 0.001 | 0.1   | 0.5 | 60  | 30  | -   | 3.2768          |
| 10  | Y  | T  | 7.5 | -2  | 1   | 0.025 | 0.05  | 0.1 | 60  | 30  | -   | 4.0331          |
| 11  | T  | Y  | 7.5 | -3.5 | 2  | 0.001 | 0.05  | 0.1 | 180 | 30  | -   | 4.0439          |
| 12  | Y  | T  | 5  | -3.5 | 2   | 0.025 | 0.1   | 0.1 | 180 | 30  | -   | 5.6506          |

### 3.3. Optimum condition of box-behnken experiment design results

The Box-Behnken design seeks the relationship between response results and factors using a sequence of experiments designed to produce the optimum response [10]. The Box-Behnken design uses 3 levels, namely the high level (+), the middle level (0) and the low level (-) values shown in each level in Table 3. Based on the Minitab 18 program, the number of measurements made for 3 parameters with 3 levels is 15 times the measurements shown in Table 4.

**Table 3.** Factor and Gd analysis level by DPV.

| Factor                  | Level    |
|-------------------------|----------|
|                         | +        | 0        | -        |
| Potential deposition    | -2 V     | -2.75 V  | -3.5 V   |
| Modulation amplitude    | 0.1 V    | 0.075 V  | 0.05 V   |
| Time deposition         | 120 s    | 90 s     | 60 s     |

**Table 4.** Box-Behnken design table 3 factors and 3 levels.

| Run | Potential deposition | Modulation amplitude | Time deposition | Response      |
|-----|----------------------|----------------------|-----------------|--------------|
| 1   | -3.5                 | 0.05                 | 90              | 6.9329E-06   |
| 2   | -2                   | 0.05                 | 90              | 3.7478E-06   |
| 3   | -3.5                 | 0.1                  | 90              | 6.1056E-06   |
| 4   | -2                   | 0.1                  | 90              | 1.1002E-05   |
| 5   | -3.5                 | 0.075                | 60              | 3.8551E-06   |
| 6   | -2                   | 0.075                | 60              | 3.8816E-06   |
| 7   | -3.5                 | 0.075                | 120             | 3.9892E-06   |
| 8   | -2                   | 0.075                | 120             | 1.0272E-05   |
| 9   | -2.75                | 0.05                 | 60              | 4.4479E-06   |
| 10  | -2.75                | 0.1                  | 60              | 7.4885E-06   |
| 11  | -2.75                | 0.05                 | 120             | 8.8464E-06   |
| 12  | -2.75                | 0.1                  | 120             | 1.0165E-05   |
From the results of data processing, factors that have a positive influence can be seen using Pareto diagrams. Based on Figure 2 shows that the parameters that show a positive influence are deposition potential, deposition time, amplitude modulation, deposition potential*deposition time, amplitude modulation*deposition potential and deposition time*amplitude modulation.

Table 4. Cont.

|   |   |   |   
|---|---|---|---|
| 13 | -2.75 | 0.075 | 90 | 7.2109E-06 |
| 14 | -2.75 | 0.075 | 90 | 7.2717E-06 |
| 15 | -2.75 | 0.075 | 90 | 7.2457E-06 |

The results of the coefficient test from the regression showed that the overall model was declared significant because it obtained a P value of less than 0.05, meaning that the model in accordance with this study was a linear model. Table 5 shows that a variable consisting of one variable shows a linear effect while a variable consisting of two variables shows the interaction effect between two variables, and the P value is used to determine the significance of each variable. For the deposition potential variable*deposition time and amplitude modulation*the deposition potential obtains a P value less than α = 0.05, indicating that the two independent variables have a very significant effect. While the P value for amplitude modulation*deposition time obtains a P value of more than α = 0.05, which indicates that the independent variable has no significant effect. For the lack of fit test, the P value of < 0.001 is smaller than α = 0.05, p this shows that there is a lack of fit in the model.

Figure 3 shows a P value greater than 0.05 (equal to 150 0.150) and concluded that failure failed to reject H0 (accept H0). This means that the residuals are normally distributed. Furthermore, to determine the accuracy of the model with the coefficient of determination test (R2), it can be concluded that the estimated value with the model is close to the value obtained from the experimental results. The smaller R2 means the relationship between the independent variables is getting weaker otherwise if R2 gets closer to 1, then the relationship between the independent variables gets stronger.

Based on the value of R2 where the percentage of the total variation obtained the value of R2 in this study amounted to 0.8563 or 85.63%. This shows the influence of the potential free deposition variable, deposition time and amplitude modulation on the response of the current generated by 85.63%, for an R value of 0.9253, and there are 14.37% influence of other independent variables that are not included in the model.
Table 5. Table of the effects of regression coefficients on the model.

| Term                                      | Coefficient | SE    | P value |
|-------------------------------------------|-------------|-------|---------|
| Potential deposition                      | 0.000001    | 0.000000 | 0.040   |
| Modulation amplitude                      | 0.000001    | 0.000000 | 0.012   |
| Time deposition                           | 0.000002    | 0.000000 | 0.003   |
| Potential deposition*Potential deposition | -0.000001   | 0.000000 | 0.032   |
| Modulation amplitude*Modulation amplitude | 0.000001    | 0.000000 | 0.131   |
| Deposition time*Deposition time            | -0.000000   | 0.000000 | 0.485   |
| Potential deposition*Modulation amplitude | 0.000002    | 0.000000 | 0.011   |
| Potential deposition*Time deposition       | 0.000002    | 0.000000 | 0.018   |
| Modulation amplitude*Time deposition       | -0.000000   | 0.000000 | 0.384   |
| Lack of fit                               | 0.000000    | 0.000000 | 0.001   |

Figure 3. Curve residual normal distribution curve.

In Figure 4, the deposition time and deposition potential have a steep rising contour plot. This means that the increase in deposition time and deposition potential will affect the response of the current generated. Based on Figure 4, which has the best response is shown by the dark green area. So it can be concluded that if the deposition potential is increased and the deposition time is increased it will provide the best current response shown in the dark green area.

Figure 4. Contour plot current response to variable deposition potential (V) deposition time (seconds).
3.4. The standard curve for Gd

The standard curve for Gd solution was made by determining the peak current of gadolinium with concentrations of 10, 15, 20, 25 and 30 mg/L in the pure water media. Measurement of the current response was done with the conditions: amplitude modulation 0.1 V; deposition potential -2.0 V; and a deposition time of 120 seconds. Based on Figure 5, the higher the concentration, the higher the peak produced can be seen at a potential of -0.3 V. The gadolinium element was reduced at a potential of -0.3 V with a reasonably good peak current and a potential shift towards a more positive direction with separation which is quite good. From the standard curve obtained $R^2$ value of 0.9939 with the acquisition of the detection limit value of 3.97 mg/L and the quantification limit of 10.71 mg/L. As well as obtaining the accuracy and precision of each concentration with three replicates is shown in Table 6.

![Figure 5: Gd voltammogram with optimum condition modulation amplitude 0.1 V; deposition potential of -2.0 V and deposition time of 120 seconds.](image)

![Figure 6: Calibration curve variations in Gd concentration (10, 15, 20, 25 and 30 mg/L) with optimum conditions of amplitude modulation of 0.1 V; deposition potential of -2.0 V and deposition time of 120 seconds](image)

| Added Gd (mg/L) | Current ($10^{-6}$ A) | Measured Gd Sb | Kv | Accuracy | Precision |
|-----------------|------------------------|----------------|----|----------|-----------|
| 15              | 3.4301                 | 14.05          |    |          |           |
|                 | 3.4256                 | 14.12          |    |          |           |
|                 | 3.4179                 | 14.58          |    |          |           |
| **Average**     | **14.25**              | **1.31**       | **1.6%** | **95.1%** | **97.76%** |
4. Conclusion
The Gd selected factor optimized using the Box-Behnken experimental design produces optimum conditions where the amplitude is 0.1 V, the deposition potential is -2.0 V and the deposition time is 120 seconds and produces a peak current at a potential of -0.3 V with a precision value of 97.76%, 95.1% accuracy, and 95% recovery.

Acknowledgments
The author would like to acknowledge the financial support from the Academic Leadership Grant Program, Universitas Padjadjaran, and the Directorate of Research and Community Service through Superior Research of Higher Education (DRPM-PDUPT) for providing the research fund under contract number 2778/UN6.D/LT/2019.

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