Quality Design and Control Tools in Nanotechnology

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Abstract: The rapid growing of nanotechnology in various fields around the world has encouraged different disciplines to develop an effective road map to improve its outputs by reducing Nano scale-wastes and errors which have significant impacts on product life-cycle. The value of these wastes and errors can be added positively to products if it is identified, measured, and controlled early in the first step of product design. Quality design and control (QDC) and their engineering tools have become a successful framework to be implemented in any industrial or manufacturing process to reduce waste and to minimize defects. Some research papers have reviewed how statistical tools have been implemented in Nanotechnology applications, but they are still few and spread around. This paper reviews how Statistical Process Control (SPC) and Design Of Experiment (DOE) are being implemented in nanotechnology to increase the production efficiency and reduce manufacturing waste and can be used a reference for those designing for typical Nano product . The results showed that the MCUSUM control chart is an effective tool that can be used in semiconductor- nonmanufacturing industry for plasma screensindustries.Also, The Hotelling's T2 and MC1 control charts are effective to detect large shift and small shift in the mean at the same timeand especially for large auto correlated data.

Introduction:

According to [1], Nanotechnology is that technology deals with materials at very small scales. These scales are called "Nano scales" that equal to one thousand times smaller than the "micro scales". By using nanotechnology, unusual physical, chemical, biological properties can be emerged. Materials, which are commonly used in this technology, are carbon, metals and metal oxides. All of these materials have negative environmental and economic impacts [2]. Nanotechnology is one of technologies that allow manufacturing many things at low cost and without pollution. Currently, nanotechnology produces food, clothes, medicine, and electronic devices such as Apple iPod [3].

The U.S Environmental Protection Agency (EPA) defined the nanotechnology as an art or since involves working on material at the atomic or molecular scale in order to provide improvements in technologies for protecting the environment [4]. The National Nanotechnology Initiative (NNI) which is comprised of "26 federal agencies, 13 of which have R & D budgets in Nanotechnology" has reported to have a development technology that can be used at the atomic scales of "Approximately 1-100 nanometer range in any direction." Also, NNI was recommended to develop a technology, which can create or use structures, devices, and systems that have unusual or novel properties and functions, with ability to control or manipulate small scales, then that technology was developed and called as Nanotechnology, as cited in [4].

George Elvin, who is the director of Green Technology Forum (GTF) has reported that some uses of nanotechnology, such as solar energies, structural materials and insulation, can help to make green building more cost- effective, energy efficient, and more " In tune with their environments." Elvin also mentioned that these uses can also help to remove, reduce, and naturalize pollutants from building's surrounding atmosphere, as cited in [5].

Not only does nanotechnology improve quality of products, but it also reduces costs associated with products that have being manufactured. In particular, nanotechnology eliminates the production of unwanted materials and pollutants, which leads to higher quality products. It also reduces wear, tear, and friction, and hence minimizes the desire for lubricant materials and cooling systems, which eventually cut costs. Despite that fact that companies adopting nanotechnology may experience higher research and development costs comparing to conventional technology, on the long term, production costs, distribution costs and quality costs are significantly reduced by considering the application of nanotechnology techniques, (see Fig. 3), [6].

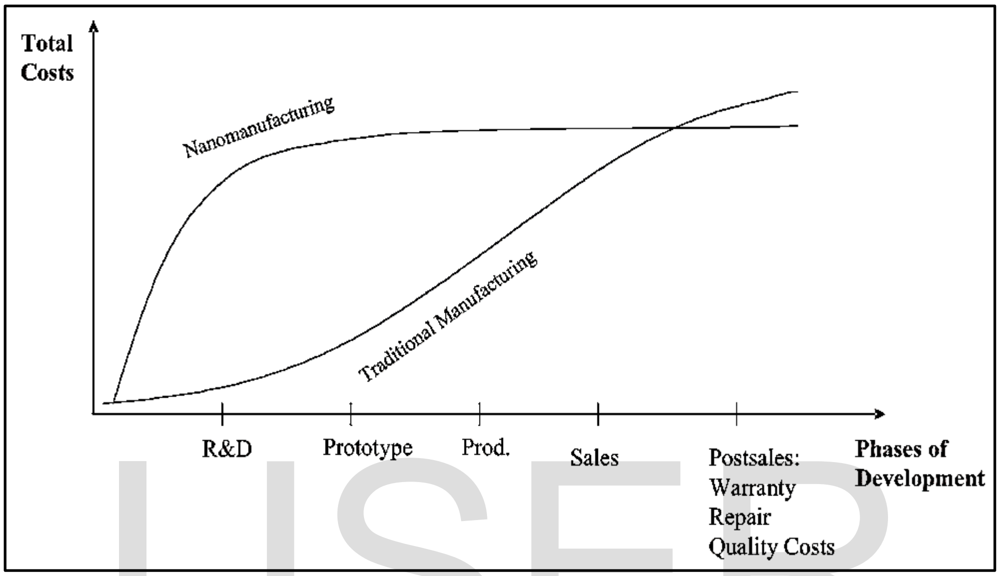

Figure 1: Life cycle cost of a product, [6]

Products manufactured by nanotechnology techniques are currently sold worldwide and are expected to generate considerable revenue in the near future. In fact, the global sales of products containing nanomaterials constituted more than $32 billion in 2005. Furthermore, it was reported that, by 2015, the global market for nanotechnology products will expand to $1 trillion [7].

One product in which nanotechnology has been implemented successfully is automobile paint. Nano-particles used in such paints have higher scratch-resistant qualities and improved surface finish due to their unique properties compared to other traditional car paints. Nanotechnology has been also successfully applied in healthcare. Nano-silver particles, for instance, are used in medical bandages to efficiently prevent infection during treatment and help skin heal faster,[7].

Many articles have been written on nanotechnology since its innovation. Lindquist, Mosher-Howe, & Liu (2010) collected articles on nanotechnology from The New York Times online database for the period from 1969 to 2007. During the period from 1985 through 1999, the average number of nanotechnology articles published by The New York Times was around 5 articles per year, (See Fig. 4). However, a significant increase in the number of articles on nanotechnology has been noticed afterwards.

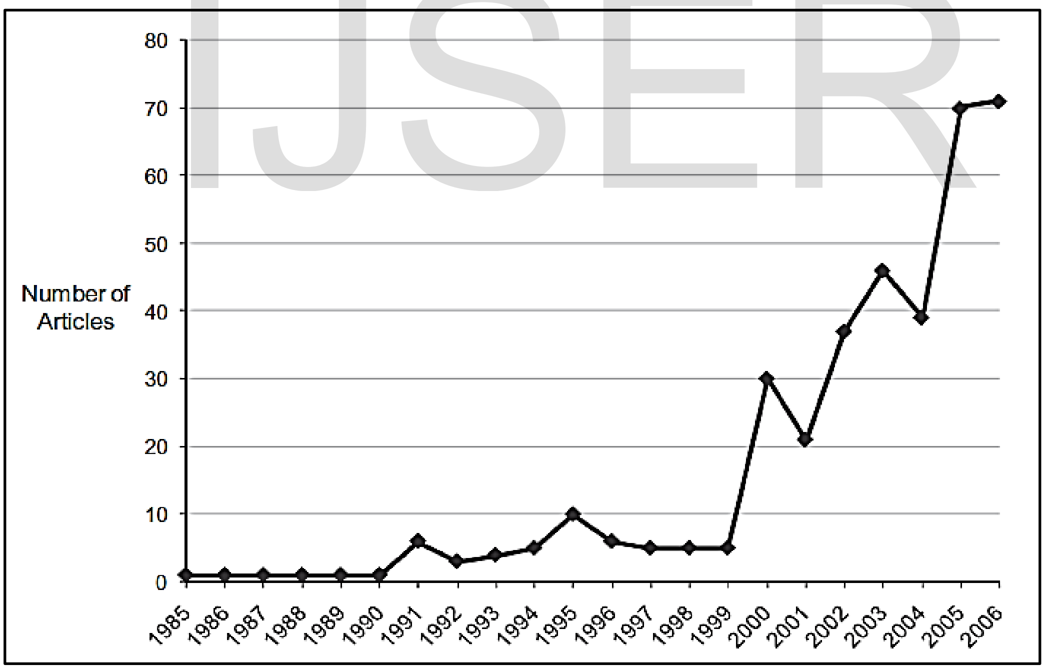

Figure 2: Number of nanotechnology articles (Lindquist et al., 2010)

Nevertheless, most of these articles focus on the size property in their definition of nanotechnology, (See Fig. 5). Only few articles shed the light on the newness and novelty of nanotechnology and its potential contribution in this area, [8]. This is a great chance for improvement by further investigating and utilizing these Nano-properties into products and services to ensure that high quality outcomes are obtained.

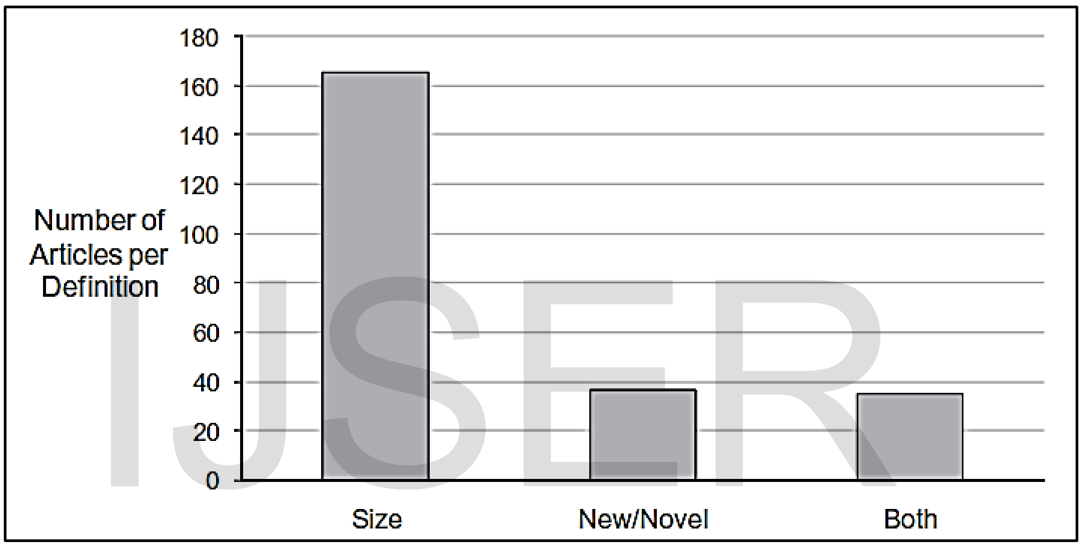

Figure 3: Number of nanotechnology articles [8]

The Beneficial of Statistical Process Control (SPC) Implementation in Nonmanufacturing

Complicated processes and precise product development stages have being conducted in nanotechnology to develop new Nano-products, such as nanowires [9]. Because nanomaterial are normally subjected to be in contact with chemicals and other materials that can change the physical and chemical properties on nanomaterial, in many cases, researchers may need to sort through the billions of nanowires and nanotubes in order to find few of them meet the required specifications [10]; [3].

In 2007, Nembhard reported that process control, reliability and repeatability of the processes and products have not been well established in nonmanufacturing. Since nanotechnology is reducing wastes, it makes no sense to have billion batches of products and only less than ten of them meet the specifications and technical requirements [3]. Therefore, fixing the issue of reproducing wastes was linked to the quality improvement processes [3] that can take into account finding the best approach to monitor processes, identify causes of errors, eliminating or reducing these causes, improve processes, and increase number of conforming products that will meet the required specifications.

In short, Statistical Process Control (SPC) has being implemented in nonmanufacturing and the results obtained from this implementation were impressive [11]. SPC was used to analyze the surface for defects by using Atomic Force Microscopy (AFM) [12], as cited in [3]. Multivariate Statistical Process Control (MSPC) methods were also implemented in nonmanufacturing in order to identify the special causes of errors by monitoring the behavior of auto correlated processes [13]. By using these methods, multivariate “Data was reduced in dimension and correlated with final product quality.”, as cited in [3]; [11].

Not only were the SPC principles have been adopted from the quality and implemented in nonmanufacturing, but also different quality standards were also developed and used in nanotechnology [3]. The ISO/TC 229- Nanotechnology is one of these standards that were developed by the International Organization for Standardization (ISO). This standard develop different standards that were listed in the ISO- website, such as ISO/TS 10797:2012 for nanotubes characterization, ISO 10801:2010 for generating of metal nanoparticles, and ISO/NP TS 12901-2 for control banding approach...etc. [14].Using SPC and quality standards in nanotechnology was considered the start of implementation of Total Quality Management (TQM) concepts, methods, and principles in nanotechnology.

In 2007, Nembhard [3], has stated a comparison between the production of nanowires, which was in many cases fewer than 10 nanowires out of 1000 on a wafer and the production of same wires with implementing Six Sigma methodology, which aims for processes that produce products that are 99.99966% defects free. Positive and aggressive results would be obtained whenever nanotechnology production processes met Six Sigma levels.

In this paper, an overview about using quality tools and methods in nanotechnology to control processes and Nano-systems was performed in order to see how the concept of QDC is important to achieve high quality Nano-products with lower cost and less time by reduce variation in processes and reproduction of errors.

Multivariate Statistical Process Control (MSPC) in Nanotechnology

Due to the complexity and intricacy of nanotechnology, SPC methods, such as multivariate exponentially weighted average method, component analysis, and profile monitoring were recently used in different Nano-process to control them and to reduce the impact of auto-correlated processes on Nano scales [3]. One of the most powerful tools that are commonly used in monitoring processes behavior over time is the control chart [15]; [16]; [11]; and [17]. Since the control charts are designed for monitoring single quality characteristic, the complexity of Nano-processes and Nano-systems that have multiple related quality characteristics which must be monitored simultaneously, new control charts are required to monitor such kind of these auto correlated processes and systems [18]. A separate univariate control charts were developed and recently widely used to monitor each quality characteristics for some complex processes [19]. However, some reasons have encouraged researchers and scientists to develop new method for monitoring auto correlated processes in nanotechnology.

In his work, [19], provided the reasons behind developing multivariate control charts and explained why they are more useful to monitor auto correlated process, such as Nano-processes than using univariate control charts. First reason is the type I error will be increased by using univariate control chart for each quality characteristic because each characteristic has its own type I error and with monitoring each of them simultaneously, the over all probability of type I error or the false alarm will be increased [19]. Another reason is the univariate control charts neglect the correlation among the multiple quality characteristic [20]; [21]. As a result, different multivariate control charts were developed in order to use them for monitoring auto correlated processes in manufacturing in which nonmanufacturing one of them. In the next sections, an overview of using multivariate control charts in nanotechnology was provided in order to introduce them with the respect to importance of using SPC in nonmanufacturing and to show how these charts were helped to reduce variation and errors in these processes.

Hotelling's T^2 Control Charts

According to (Hotelling, 1947), One of the earliest method for monitoring multivariate processes are Hotelling's T^2 control charts, as cited in [13]. This kind of control chart is commonly employed by assuming the covariance of quality characteristic is unknown [19]; and [18].If we compare the calculations of Hotelling's T^2 control charts with Shewhart's control charts, we will find Shewhart's control charts is much easier to construct than Hotelling's control charts. However, in some studies, Hotelling's T^2 control charts were used and the results showed that these charts were effective to monitor autocorrelation among quality characteristics [19]. With knowing the covariance matrix for each quality characteristic, the X^2 statistic is used to construct Hotelling's T^2 control charts [18]. There are three types of Hotelling's T^2 control charts and each of these types has specific conditions to construct. These types are known as the usual T^2 control chart, the T^2 control chart with Minimum Volume Ellipsoid (MVE) estimators, and T^2 control chart with S estimators. Studies showed that for a small number of observations, control chart with S estimators performs better than the other two charts. However, with increasing in the number of observations, T^2 control charts based on S and (MVE) estimators perform similarly. In any case, with the presence of outliers, robust control charts should be used instead of the Usual T2 control chart [22].

MEWMA- Control Charts

The rapid development in Nanotechnology and other modern technologies provides some auto correlated data that can be used to develop methods for monitoring processes and control them properly [13]. In recent research, SPC have been developed for monitoring auto correlated data in some industries to reduce variation in their processes that would be caused by existing of special causes [18] Multivariate Exponentially Weighted Moving Average (MEWMA) control chart is one of SPC tools that could be used for controlling auto correlated processes and systems [21]; and [23]. These charts are able to detect the small and rapid shift in the process mean as reported in [24]. Also, it was considered as the base model that was used to develop new control charts to detect the autocorrelation in processes and to monitor the special causes of out of control processes [13]. Base on MEWMA control charts, the Multivariate Cumulative Sum control charts (MCUSUM) were proposed and constructed by [25]. It easy to construct, but the only problem that has reported was these charts were unable to detect the sudden large shift in the mean [18].

Auto correlated Control Charts Validation and Comparison:

In order to validate the work of the above two control charts for the auto correlated processes, further literature review was performed in order to gather as much as possible of data about them to answer some important questions, such as, which of them is able to detect the small shift in the mean? And which chart can detect the sudden large shift in the mean?

In their work, [26] proposed two types of MCUSUM control charts which were named as MC1 and MC2 control charts, as cited in [18] The Markov Chain approach and a Monte Carlo simulation were used to compare the performance several schemes for monitoring a multivariate normal processes. The average run lengths of MCUSUM charts and Shewhart X^2 charts were compared to the average run lengths for the MC1 and MC2 control charts. The overall comparison between the performances of these proposed control charts were provided in below:

- Detecting small shifts in the mean vector from the MCUSUM control chart and MC1 control chart are better than that of Hotelling's T^2 control chart.
- When there is a sudden large shift in the mean, the performance of Hotelling's T^2 control chart is better than that of MCUSUM control charts.
- The average run length of MC1 is more stable than the other three control charts
- Hotelling's T2 control charts are sensitive to small shifts in the mean vector.

In his study [13], the MCUSUM control charts were used to monitor specific processes in nonmanufacturing as demonstrated in following:

The MCUSUM control chart was used in semiconductor- nonmanufacturing industry for plasma screens. Several important variables were involved in this kind of manufacturing, but the most significant process variables that affect the process quality were identified and there were two variables. The generate powder (PG.) variable and the fluorine line intensity (IF) variables were considered important and need to be monitored during the production processes of Plasma screens. These variables followed bivariate normal distribution with mean vector and specific covariance matrix. The collected samples about these two variables were highly correlated due to the relationship between them.

With control limits equaled to +3.35, - 3.35 and Average Run Length (ARL) equaled to 200, the mean shift signal is detected in 15 observations, see the following figure:

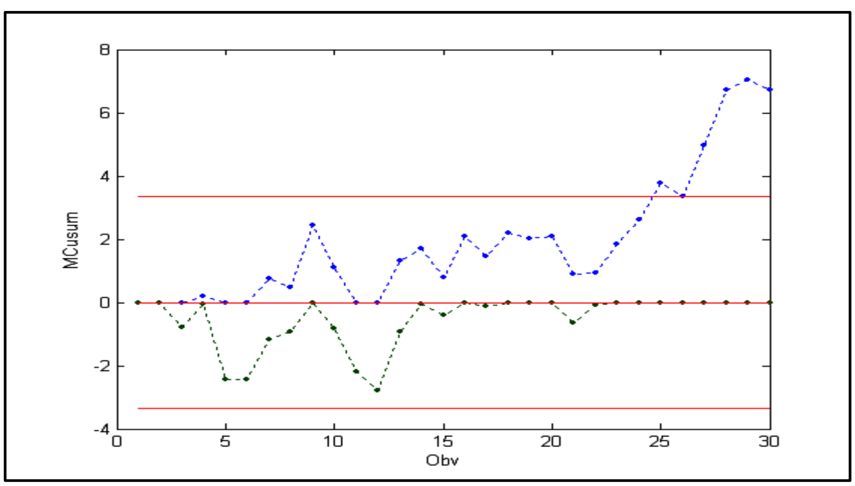

Figure 4: The residual-based MCUSUM chart for PG and IF.as adopted from [13]

The auto correlated processes require special and effective SPC to monitor them and to identify the special causes of errors. From the investigation of literature in above, we can conclude that the Hotelling's T^2 and MC1 control charts are effective to detect large shift and small shift in the mean at the same time. Also, the MCUSUM control chartis good to detect the small shift in the mean vector for the large auto correlated data. All of these control charts are considered to be effective to monitor Nano-processes which are auto correlated processes in order to fix problem at the first stage of new Nano-product development life cycle

DOE in Nanotechnology

The most successful way to improve product or service quality and reliability is to combine them in the design process. Design of Experiments (DOE) is a practical tool that can be implemented in the early phases of the development cycle. Experimental design is a successful method for increasing the data added from a study although minimalizing the collected information.Factorial experimental designs study the effects of various factors by changing them simultaneously instead of varying only one factor at a time. Factorial designs estimates the sensitivity of every factor, and it also study the combined effect of multiple factors, [17].

DOE is applicable to both physical developments and simulation. Experimental design methods have been effectively adopted by many industries, such as automotive, medical product, etc. The application of DOE is not limited to engineering. It has been successfully applied to many areas, and it has been recently considered in many Nano-scale quality improvements. Design of experiments can be used for many purposes such as: comparisons, variable screening, transfer function exploration, system optimization, and system robustness. Comparisons when several design selections are considered, and when several materials or suppliers are available. Variable screening; for a large number of variables that may affect the system or how a product is performing, but only a relative small number of them are significant, a screening experiment also can be conducted to identify the significant variables, [27].

Transfer function exploration; the transfer function is a relationship between the output response and input variables. DOE can be applied to design efficient experiments to study the linear and quadratic effects of the variables and some of the interactions between the variables. System Optimization; the objective is to improve the performance, like improving, quality and reliability. DOE delivers a bright strategy that optimizes the sitting of variables of any experiment. Robust design is one of the most important DOE techniques, [28].

DOE has been used as a key tool for studying the relation between process responses and controllable factors. Different designs have been used for different experiment reasons. The following list shows the generally used design forms, [27].

1. For comparison
    - One factor design

2. For variable screening
    - 2 level factorial design
    - Taguchi orthogonal array
    - Plackett-Burman design

3. For transfer function identification and optimization
    - Central composite design
    - Box-Behnken design

4. For system robustness
    - Taguchi robust design

The design that used for transfer function identification and optimization is termed Response Surface Method designs. In this research paper, we will give attention to the two most popular and basic designs which are two-level factorial design and two-level fractional factorial design.

As a result of growing demand and applications in Nano-electronics, photonics, data storage, and sensing, synthesizing nanostructures is a research topic of primarily significance in nanotechnology [28]. Nevertheless, the structure process is very sensitive to control settings and environmental noise. With a view to robustly improve some properties of Nano-products, the effect of every factor, and their interactions, on the outputs must be considered with the help of powerful statistical tools and methods.

DOE method is one of these practices of quality design and control that has being recently used in nanotechnology. The robust design in Nano-technology had been reviewed by [28]. In his dissertation and he introduced examples of how these methods could be employed in the Nano-manufacturing processes. For example, he mentioned that "to generate the nanostructures of Nano-saws, nanowires, and Nano-belt, the control factors, such as temperature and pressure, have a heavy impact on the final output of a synthesis process. Moreover, situations occur in which multiple responses are studied with functional relationships containing many potential factors of interest". In order to strongly improve many properties of Nano-products, the effect of every factor, and their interactions, on process outputs must be reviewed by more advanced statistical techniques, [27].

Implementation of DOE methods in Nano-technology

In this part, we will take a glance of some new studies that applied DOE in the research and development of Nano-product using second level factorial design; results have been found and discussed by the authors for each case.

DOE for synthesizing in situ Ni–SiO2 and Co–SiO2 Nano-composites by non-isothermal reduction treatment was summarized as in following:

In their work, [29], investigated how the DOE used to synthesis processes for Ni–SiO2 and Co–SiO2 in Nano-composites, of which the physical aspects are extremely sensitive to processing parameters, which makes the response surface extremely rugged. Since these conditions have critical effect on the characteristic of Nano-composites, authors investigated that the experiments were made according to a statistical experimental designs. A regression equation is molded from which the influence of each process variable and its relative impact on the process can be easily evaluated. Moreover, the impact of the interaction of multiple variables can be interpreted clearly than before. The variable process parameters and their selected range are shown in Table 1. The design matrix and the results showing fractional conversion (α) of NiCl2 to Ni and CoCl2 to Co are shown in Table 2.

Table 1: Actual and coded values of the variable parameters for the silica gel containing NiCl2 and CoCl2 respectively. [29]

	Initial temperature		Heating rate		Weight per cent metal in SiO_2 matrix	
Levels	Actual x_1 (°C)	Coded X_1	Actual x_2 (°C min^{-1})	Coded X_2	Actual x_3	Coded X_3
Upper	600	+1	10	+1	10	+1
Lower	500	−1	4	−1	5	−1
Base	550	0	7	0	7.5	0

Table 2 : Design matrix and results of non-isothermal reduction of silica gel containing (A) NiCl2 and (B) CoCl2[29]

Sample identity of gels containing								Fractional conversion of gels containing	
$NiCl_2$	$CoCl_2$	X_1	X_2	X_3	X_1X_2	X_1X_3	X_2X_3	$NiCl_2$	$CoCl_2$
SN-1	SC-1	−1	−1	−1	+1	+1	+1	0.6857	0.4035
SN-2	SC-2	−1	+1	−1	−1	+1	−1	0.3863	0.1241
SN-3	SC-3	−1	−1	+1	+1	−1	−1	0.5254	0.4027
SN-4	SC-4	−1	+1	+1	−1	−1	+1	0.2476	0.1184
SN-5	SC-5	+1	−1	−1	−1	−1	+1	0.8947	0.6061
SN-6	SC-6	+1	+1	−1	+1	−1	−1	0.4922	0.2917
SN-7	SC-7	+1	−1	+1	−1	+1	−1	0.7136	0.5768
SN-8	SC-8	+1	+1	+1	+1	+1	+1	0.3262	0.2740
SN-9	SC-9	0	0	0	0	0	0	0.5556	0.3414
SN-10	SC-10	0	0	0	0	0	0	0.5081	0.3572
SN-11	SC-11	0	0	0	0	0	0	0.5330	0.3628

The authors designed eleven runs using a 2-level full factorial design. Using regression equations fitted by the 11-run experiment outcomes, the fractional conversion values of the Nano-composites were formed as a function of the initial temperature, heating rate and weight percent metal to be liberated by non-isothermal reduction were considered as input variables. The regression equation for the matrix is explained as:

$$\alpha = a_0 + a_1 X_1 + a_2 X_2 + a_3 X_3 + a_{12} X_1 X_2 + a_{13} X_1 X_3 + a_{23} X_2 X_3 + \cdots \quad (1)$$

Test of significance using t -test with 95% confidence level showed that only the coefficients a0, a1, a2 and a3 are significant for preparing Ni– SiO2 Nano-composites. Therefore, the final regression equation for Ni–SiO2 is represented as

$$\alpha\,(Ni) = 0.5340 + 0.0727X_1 - 0.1709X_2 - 0.0807X_3 \ldots \quad (2)$$

The relationships between the coded values and the actual values are given as

$X_1 = (x_1 - 550)/50$; $X2 = (x_2 - 7)/3$; $X_3 = (x_3 - 7.5)/2.5$

Substituting the values of $X1\ X2\ X3$ in equation (2) gives:

$$\alpha\,(Ni) = 0.5340 + 0.0727(x_1 - 550)/50 - 0.1709(x_2 - 7)/3 - 0.0807(x_3 - 7.5)/2.5 \ldots \quad (3)$$

Similarly testing the significance using t -test with 95% confidence level showed that only the coefficients a_0, a_1 and a_2 are significant for preparing Co–SiO2 Nano-composites Therefore, the final regression equation obtained for Co–SiO2 Nano-composites is: $\alpha(Co) = 0.3497 + 0.0875X_1 - 0.147X_2 \ldots \quad (4)$

Substituting the values of $X1\ X2\ X3$ in equation (3) gives:

$$\alpha\,(Co) = 0.3497 + 0.087(x_1 - 550)/50 - 0.1709(x_2 - 7)/3 \ldots \quad (5)$$

Using equations (3) and (5) fractional conversion values of Ni–SiO2 and Co–SiO2 Nano-composites can be successfully predicted for all the possible values of the variable process parameter that lie within the selected domain of the experiments. It is also evident from the regression equation that the effect of heating rate is the most predominant factor. A comparison of the predicted values and experimental values of fractional conversion of Ni– SiO2 and Co–SiO2 is shown in Table 3 and figure 1.

Table 3: Results of experimental and predicted fractional conversions of gels containing NiCl2 and CoCl2. [29]

	Heating rate (°C min^{-1})		Wt% metal in SiO_2 matrix		Predicted α values		Experimental α values	
No of obs.	Ni/SiO_2	Co/SiO_2	Ni/SiO_2	Co/SiO_2	Ni/SiO_2	Co/SiO_2	Ni/SiO_2	Co/SiO_2
1	9.52	8.33	5	5	0.5436	0.3912	0.5389	0.3711
2	7.40	6.66	5	5	0.6641	0.4796	0.6458	0.4452
3	5.13	5.13	5	5	0.7939	0.5611	0.8073	0.5352
4	9.52	8.33	10	10	0.3805	0.3913	0.3697	0.3560
5	7.40	6.66	10	10	0.5027	0.4798	0.4554	0.4178
6	5.13	5.13	10	10	0.6325	0.5611	0.6027	0.5314

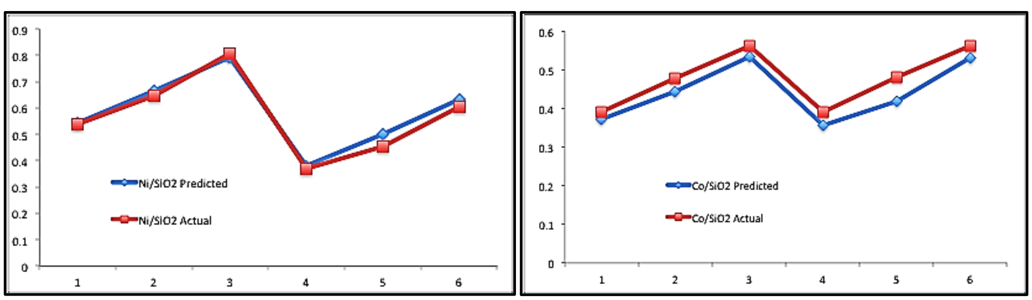

Figure 5: Predicted vs. experimental in NiCl2 and CoCl2.

As per the authors conclusion "regression equations modeled using the statistical experimental design can be successfully used to predict the fractional conversion values of the metal chloride containing SiO2 gel to the in situ Nano-composites as a function of heating rate, metal chloride concentration and starting temperature of the reaction. The regression equations for the Ni–SiO2 and Co–SiO2 Nano-composites indicate that the fractional conversion of metal chloride to metal increases with the increase in the starting temperature of the non-isothermal heat treatment. However, the rate of heating (for both the Ni–SiO2 and Co–SiO2 systems) and the amount of metal chloride in the gel matrix (only for the Ni–SiO2 system) has been found to exert a negative influence on the fractional conversion". [29]

Optimization of Polylactic-Co-Glycolic Acid Nanoparticles Containing Itra-conazole Using 2^3 Factorial Design

In 2003, Prakobvaitayakit and Nimmannit used solvent displacement technique to prepare polylactic-co-glycolic acid (PLGA) nanoparticles. They used design of experiment techniques such as a 2^3 full factorial design and response surface methodology (RSM) to optimize the nanoparticles of PLGA. Three input variables namely, the concentration of PLGA, benzyl benzoate, and itraconazole were considered in the experiment. Similarly, three responses: particle size, the amount of itraconazole entrapped in the nanoparticles, and encapsulation efficiency were defined.

To determine the effects of the independent variables and their interactions on the responses, the analysis of variance (ANOVA) approach was used. Each individual variable was evaluated based on p-value or F test as shown in Table 4. After significant factors have been identified, the response surface methodology (RSM) was used to construct a mathematical model for each response. The experimental results showed that the concentration of PLGA, benzyl benzoate, and itraconazole have great impact on particle size, the amount of itraconazole entrapped in the nanoparticles, and the encapsulation efficiency, [30].

Table 4: Data analysis of PLGA nanoparticles, [30]

Parameters	Size (nm)		Encapsulation Efficiency			
			ITRAe (μg/mL)		ITRAe (%)	
		P Value		*P* Value		*P* Value
Model	F = 3108.78	<.0001	F = 19 369.93	<.0001	F = 1314.44	<.0001
B_0	373.75	<.0001	472.93	<.0001	57.36	<.0001
B_1	66.54	<.0001	73.45	<.0001	6.53	<.0001
B_2	52.09	<.0001	169.06	<.0001	15.52	<.0001
B_3	105.06	<.0001	333.03	<.0001	−12.59	<.0001
B_{12}	−4.73	.0006	0.086	.9397	−0.14	.5261
B_{13}	46.30	<.0001	62.40	<.0001	1.01	.0006
B_{23}	1.50	.1716	141.49	<.0001	1.73	<.0001
B_{123}	1.19	.2721	0.75	.5121	0.19	.4051
Error MS	17.03		19.92		0.78	
Curve MS	30 290.62	<.0001	12 052.00	<.0001	657.38	<.0001
$F_{curvature}$	1778.94		10 300.13		847.52	
R^2	0.9994		0.9999		0.9987	
Adjusted R^2	0.9990		0.9999		0.9979	
CV	1.04		0.84		1.46	

*CV indicates coefficient of variation; F, F Value; ITRAe, the amount of itraconazole entrapped in the nanoparticles; MS, mean square; and R^2, determination coefficient.

Diameter optimization of VLS-synthesized ZnO nanowires, using statistical design of experiment

In 2007, Shafiei, Nourbakhsh, Ganjipour, Zahedifar, and Vakili-Nezhaad investigated the process of synthesizing zinc oxide (ZnO) nanowires through a vapor-liquid-solid (VLS) growth method. They used a two-level fractional factorial design (FFD) with resolution III (2_{III}^{6-3}) to obtain eight runs instead of using the full factorial design method which would yield a total of 26 = 64 runs. The authors considered six independent variables, namely synthesis time, synthesis temperature, thickness of gold layer, distance between ZnO holder and substrate, mass of ZnO, and Ar flow rate. These variables were analyzed to determine potential effects on the average diameter of a ZnO nanowire (response). To identify the parameters that control the process, the main effects of the independent variables are shown in Table 5, [31].

Table 5: Effects of input variables on the response, [31]

Parameter	Effect	SS	Contribution (%)
A: synthesis time	107	22898	34.86
B: synthesis temperature	-62.5	7812.5	11.89
C: thickness	126	31752	48.34
D: distance	-4.5	40.5	0.062
E: mass of ZnO	38	2888	4.4
F: Ar flow rate	3.5	24.5	0.037

It can be seen from Table 5 that synthesis time (A) and thickness of gold layer (C) are the most significant parameters. In addition, synthesis temperature (B) has a moderate effect while distance between ZnO holder and substrate (D), mass of ZnO (E), and Ar flow rate (F) have insignificant effects, and hence they were eliminated. The ANOVA was then used to develop a mathematical model, including significant parameters (see table 6). It was concluded that changing synthesis temperature from its high level to its low level causes the diameter of ZnO nanowires to decrease considerably. Furthermore, an increase in either the gold layer thickness or synthesis time would result in increasing the diameter of ZnO nanowire, [31].

Table 6: ANOVA for ZnO nanowire[31]

Factor	SS	P value
A	1.075E−005	<0.0001
B	4.113E−006	<0.0001
C	1.399E−005	<0.0001
AB	5.337E−007	0.0433
BC	4.650E−007	0.0542
C^2	4.940E−007	0.0502
R-squared = 0.9682		

Optimization of CCVD synthesis conditions for single-wall carbon nanotubes by statistical design of experiments (DoE)

In 2005, Kukovecz, Mehn, Nemes-Nagy, Szabo, & Kiricsiused design of experiments to optimize the catalytic chemical vapor deposition (CCVD) synthesis for single-wall carbon nanotubes. Seven parameters, namely catalyst composition, catalyst amount, reaction temperature, reaction time, preheating time, C_2H_2 volumetric flow rate, and inert gas volumetric flow rate were chosen. In addition, two responses: carbon deposit (C %) and quality descriptor number (QDN) were considered in the experiment, [32].

. Using a two-level fractional factorial design (FFD) with resolution III (2_{III}^{7-4}), the authors were able to set eight runs instead of 2^7 = 128 runs. The goal was to identify the key parameters that control the process, and eliminate the unimportant variables. The main effects of each parameter on both responses were investigated (see Figures 6 and 7) using main effects plots, [32].

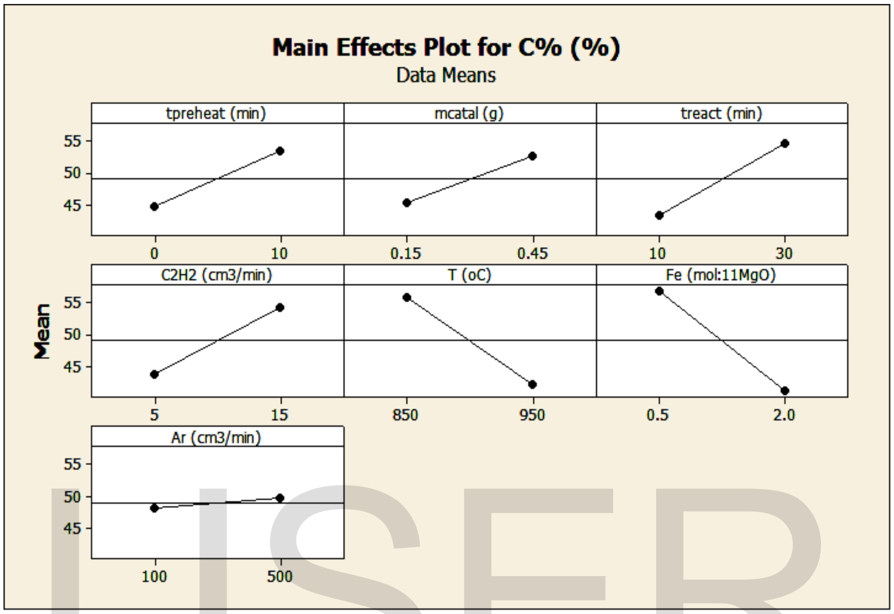

Figure 6: Main effects of input variables on C %, [32]

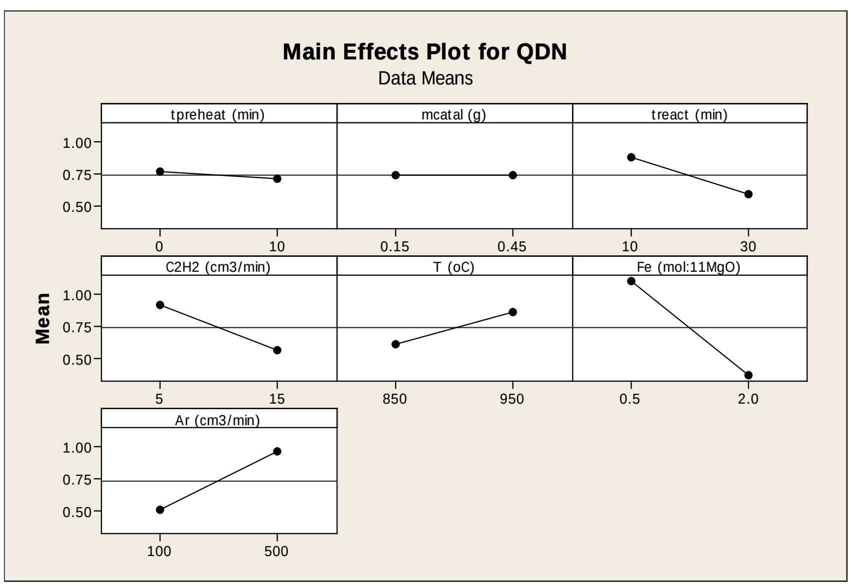

Figure 7: Main effects of input variables QDN, [32]

The results of the experiments, as illustrated in figures 5 and 6, showed that “Fe: MgO ratio” and “reaction temperature” have significant effects on both QDN and C%, so they were chosen for further optimization. “Ar volumetric flow rate” was also chosen as a third variable. A new set of data was then collected for the three selected variables, and a total of 13 runs were made. After that, an analysis of variance (ANOVA) approach as well as a three-level Box-Behnken design was implemented to develop a fitted model of both responses. It was also determined that process variables at Fe: MgO = 0.149, T = 863 C, Ar flow = 372 cm3/min yields the optimum predicted values of the responses, QND and C% were 1.40 and 55.57%, respectively, [32].

RESULTS

1. Statistical Process Control (SPC) implemented in Nanotechnology helps to identify the design error at the early stages of the product life cycle.

2. Since the control charts are effectively monitor the process behavior over the time, it is necessary to be used in order to check the process and see if it is on control or not. The MCUSUM control chart is an effective tool that can be used in semiconductor-nonmanufacturing industry for plasma screensindustries.

3. The Hotelling's T^2 and MC1 control charts are effective to detect large shift and small shift in the mean at the same time. Also, the MCUSUM control chartis good to detect the small shift in the mean vector for the large auto correlated data

4. Design of Experiments is a new approach to be implemented in order to select the optimum conditions which are highly affect the design process. Identifying the major and minor factors that could affect the quality of Nano products throughout designing an experiment helps to reduce errors, wastes, and rework or redesign to solve any particular problem. The goal is to identify the key parameters that control the process, and eliminate the unimportant variables

5. The design objective and the success factor of designing new Nano- products can be assigned properly based on the historical data that are already tested and measures. And that would help to setup new operational conditions that assure the quality of the products with avoiding the steps that might increase wastes or produce errors.

CONCLUSION

QDC tools and methods have not widely used in nanotechnology. Implementation of Statistical Process Control (SPC) and Design Of Experiment (DOE) have being noticed in some work within nonmanufacturing. Continuous improvement for nanotechnology is not limited, and QDC will be the cornerstone of this improvement.

Nanotechnology requires having effective and precise tools that could be used to produce high quality Nano products without errors and wastes. The auto correlated processes require special and effective SPC to monitor them and to identify the special causes of errors. From the investigation of literature in above, we can conclude that the Hotelling's T^2 and MC1 control charts are effective to detect large shift and small shift in the mean at the same time. Also, the MCUSUM control chartis good to detect the small shift in the mean vector for the large auto correlated data. All of these control charts are considered to be effective to monitor Nano-processes which are auto correlated processes in order to fix problem at the first stage of new Nano-product development life cycle.

This article has reviewed some instances where experimental design methods have been successfully applied. Such methods include a two-level full factorial design, a two-level fractional factorial design, and analysis of variance (ANOVA). As processes in nanotechnology are very sensitive to parameter settings and noise factors, designing an experiment considering a careful definition of controllable variables and responses is a key role in obtaining a sound and valid results. In future nanotechnology research, other design of experiment methods such as response surface, Box-Behnken design, and Taguchi robust design may be considered. Equally important are methods such as Six Sigma, certain types of control charts, and computer simulation.

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