# Experimental Planning Factorial: A brief Review

Magno de Oliveira<sup>1</sup>, Valéria MM Lima<sup>2</sup>, Shizue Melissa A. Yamashita<sup>3</sup>, Paula Santos Alves<sup>4</sup>, Augustus CaeserFranke Portella<sup>5</sup>

<sup>1</sup>Master in Biotechnologyatthe Federal University of Tocantins – Gurupi Campus-TO;

<sup>2</sup>Masterstudent in Biotechnologyatthe Federal University of Tocantins - Gurupi Campus-TO,

<sup>3</sup>Masterstudent in Biotechnologyatthe Federal University of Tocantins - Gurupi Campus Federal University of Tocantins,

GurupiCampus-TO. Embrapa GeneticResourcesandBiotechnology, Brasília - DF.

<sup>4</sup>Masterstudent in Biotechnologyatthe Federal University of Tocantins - Gurupi Campus-TO,

<sup>5</sup>TeacheroftheGraduateProgramBiotechnologyofFederlUniversityof Tocantins-Gurupi Campus-TO, PPGBiotec. Scholarship CNPq. Email:portella@uft.edu.br

Abstract— The optimization of experimental relevance parameters can be considered one of the most critical steps in a scientific work according to the chosen model may contribute to a result that does not match the true great. Thus, it is of utmost importance to the observation of the effects of the variables and the interaction between them in a given system, and the multivariate optimization systems, based on factorial design of experiments, a useful and simple alternative, given the need to assess simultaneously the effect of a large number of variables and their interaction between them from a small number of trials. In this paper, we present concepts related to optimization of multivariate procedures with emphasis on experimental design systems experiments and their application in studies of various areas of knowledge, proving its efficiency in the analysis of multivariate systems. Inclusion criteria for articles were: original articles and research on factorial experimental design in common use in laboratories in different fields of research, including studies and pre-installation already installed and in Portuguese, English and Spanish.

Keywords— Factorial design, experimental planning, multivariate analysis, factorial experiment.

## I. INTRODUCTION

Perhaps one of the most critical stages of a scientific work is related to the optimization methodology of experimental parameters of relevance. According to the methodology chosen is not always possible to evaluate the interaction between the variables and may contribute to a result that does not match the great or true. then make use of methodologies factorial experimental designs that can analyze multiple variables at the same time to the same factor (CUNICO, 2008; PERALTA-ZAMORA, 2005).

Freund; Wilson; . Mohr, (2010a) and Dias-Mayer et al, (2017), points out that the methodological systems

planning of the experimental projects, the methods must be carefully analyzed, being sophisticated techniques with statistical experiments (ANDERSON; WHITCOMB, 2010), for the purpose of collectionr data or evidence has the objective of contributing to an investigator to exercise knowledge about one or more questions about his work.

To better understand the processes that are being monitored in a particular research is of utmost importance to the observation of the effects of the variables and the interaction between them (NETOet al 2007;. PEREIRA FILHO et al., 2002). In this sense, the optimization of multivariable systems have shown great momentum and is useful in various fields of knowledge, received attention in studies involving biotechnological processes (PERALTA-ZAMORA et al. 2005).

Moura et al (1999) mention about the advantages of employing a multivariate analysis on the recognition of genetic mismatch along allow identification of genetic variability sources, the size of each character analyzed for genetic divergence as well as the levels of P (phosphorus) more appropriate, in addition to the best combinations with greater chances of success for crosses.

In their study, the authors mentioned above, investigated the feasibility of multivariate analysis to identify sources of genetic variability among lines of sweet pepper, whereas nutritional efficiency R and the most appropriate doses, as well as the most appropriate feature of the plant to the selection process.

Silva et al (2016) was used in multivariate analyzes together exploratory study units known as clustering. A hierarchical method with main components to assess the associations between the production components and product doses Ribumin, a conditioner of soil, applied in corn cultivars. The purpose of the multivariate analysis technique for grouping is to gather the sample units and groups so that there is homogeneity within the group and heterogeneity between them.

However, multivariate optimization systems, based on factorial design of experiments, have proven a useful and simple alternative given the need to simultaneously evaluate the effect of a large number of variables and the interaction between them from a small number of trials (PEREIRA FILHO et al 2002;. PERALTA-ZAMORA et al 2005;. CUNICO et al 2008)..

Freund; Wilson; Mohr, (2010b) points out that in the factorial experiment is expected to examine the effect of two or more causes the same type of sampling unit. On a study laboratory factorial experiment can be utilized to analyze the differences in the yields of several varieties, as well as the different levels of function of a microorganism, for example. A model in each combination in all levels of factors are applied TheIt is experimental units. From this perspective, understand and project the statistical control of all experimental units of a sample leads to excellence of quality of processes of goods and services of the final product to be desired.

to get nenot score in results of surveys algorithms require data simultaneously applying several factors for each experimental unit in a biotechnology laboratory it is necessary to check its quality and veracity, using bases STATISTICSatto validate the survey data to be indexed. Thus, the process of Experimental Planning Factor, it is an essential factor for the development of work in order to mitigate errors in front of tests to a job (FREUND; WILSON, MOHR, 2010b; LEARDI, 2013).

The Experimental Planning Factor It is one statistical tool that can be usedgives to check the logic of the real synthesis method and establish whether it is necessary to revalidate the tests used to access the data provided in a search. A factorial experimental design defines the imposition to make changes in the data production of synthesis in order to establish control of processes such as monitoring and control of processes with the purpose of detecting possible upgrades in the development and processes of research tests. Additionally, it assists in taken preventive decisions, becoming thus intended action to eliminate the possible causes of an impending shift of an unwanted situation in order to prevent these causes can come actually to occur (ANDERSON; WHITCOMB, 2010; FREUND; WILSON, MOHR, 2010a, 2010b).

Anderson; Whitcomb (2010); Bishop; Petersen; Trayser, 1982; Day-Mayer et al. (2017) having a factorial experimental design is to have a tool that allows to investigate each sample tested during the research meeting the requirements of procedures and protocols used by the researcher, in which, prior to testing, if performed a bibliographic. EssThe review should have a focus at synthesis dquality systems, to demonstrate that what isThe producing or being analyzed has been previously validated even if the work is unpublished, demonstrate that to then have the final product quality. Research requires adequate statistical power, sufficient sample to detect scientifically sound effects (JAN &SHIEH, 2016).

#### **1.1 Multivariate Analysis Tools**

According Bracarense; Takahashi (2014) and Anderson; Whitcomb (2010) by joining one factorial design becomes important to its use as a part of a gradual improvement process to identify areas of stress that can be allocated effectively. Factorial Experiments are tools like ANOVA, DOE, factorial design 2k, 3k or Periodic Review product (RPP), among others factorial experimental designs that can evaluate possible unwanted situations that the experiment could suffer.

ANOVA can be used to estimate the main effect of each variable and the interactions between them. The main effect is the difference between the average response of a particular variable in a level and this average response at another level, collapsing on the levels of all other variables (COLLINSet al., 2014). The analysis of variance (ANOVA) is considered the best approach when it is desired to relate various means (BOAVENTURA et al., 2017).

But the design of experiments (DOE) provides a conceptual interface through research that disrupt a phenomenon in order to understand their behavior andIt is a way to understand the process through the establishment of mathematical relationships from beginning to end of the process (POLITIS et al., 2017; BESSERIS, 2013). Such planning is also an indispensable apparatus in any scientific endeavor that requires information collected Validation (BESSERIS, 2013). Efficiency and effectiveness in designing, collecting and explain the experimental observations are essential in many areas, from engineering to management, providing a solid foundation as the main tactic of research in the physical sciences, health and social (DEJAEGHER & VAN DER HEYDEN 2011, KNIGHT et al., 2012, OBERG & VITEK, 2009).

DOE is a statistical method to establish which variables are important in the process and in what conditions these variables should work in order to optimize the process (ILZARBE et al., 2008). Its fundamental structure for implementation as well as its conversion project and interpretation of data were established by FISHER & BENNETT (1990).

More broadly, an experiment can be defined as a procedure in which a system or process purposeful changes are made to variables in order to come to evaluate the possible undergone changes due to the response variable, as in order to analyze the changes their reasons. The design of an experiment is the process of planning and executing an experiment. The statistical experimental design point is defined as the set of instructions to assign observational or experimental treatments units (FREUND; WILSON; MOHR, 2010a, 2010b).

Any experiment planning first begins with the definition of objectives, subsequently determined how it

will measure performance and finally we list the controllable factors that can affect performance (KENETT; STEINBERG, 2014).

According Kenett and Steinberg (2014), for an experiment to be considered statistically designed, some issues require determination (Table 1).

	Questions		
1	Definition of the problem; Description of the problem of language, as was the		
	identification, who is responsible for product / process consideration.		
2	response variable; What and how will be evaluated; how data will be collected.		
3	control factors; What factors can be controlled by the analyst, or planning decisions.		
4	<i>factor levels;</i> What are the levels of current factors and what are the reasonable alternatives.		
5	<i>noise factors;</i> What factors can not be controlled during regular situations, but can be controlled in an experiment, and what factors simply can not be controlled, but can be observed and recorded.		
6	<i>experimental matrix;</i> What are the main effects and interactions of interest. What is the total number of runs of the experiment. What is the power required detection against which alternatives. What are the experimental conditions.		
7	<i>Number of repetitions of the experiment and order;</i> What is the maximum number of replications in each experimental run. In which order experiment will be conducted.		
8	Data analysis; How will data be analyzed? Who will write the final report.		
9	<i>Budget and project control;</i> Who is responsible for the project. What is the budget. How will the calendar. What resources are needed.		

Table.1: Issues to consider in an experiment planning.

Note. Adapted from (KENNET; Steinberg, 2014).

The experimental design separates into two distinct phases: 1) screening phase (screening phase) and 2) modelingphase (phasemodeling) (BOXet al, 2005).. During the screening process, a group of variables receives a consideration stochastic based on their power levels shown from one or more response (MONTGOMERY, 2006). Only statistically dominant effects are introduced to the modeling phase. Screening can help make the information acquisition costs and more manageable knowledge (THOMKE, 1998).

For screening experiments, we consider the maximum possible variables(WANG, 2007)And once the

screening is completed the important factors are selected and studied through the use of more complete designs which include designs three factor levels and able to withstand the effects of quadratic growth or higher(POLITIS et al., 2017). However, in manufacturing processes it is necessary to explore some of the interactions between two factors taken into account for this, are chosen projects that are able to assess the interaction between these two factors. Being able to use the expertise in related fields and draw the experiment considering these interactions and leaving it to find the best design for the experiment(WANG, 2007).

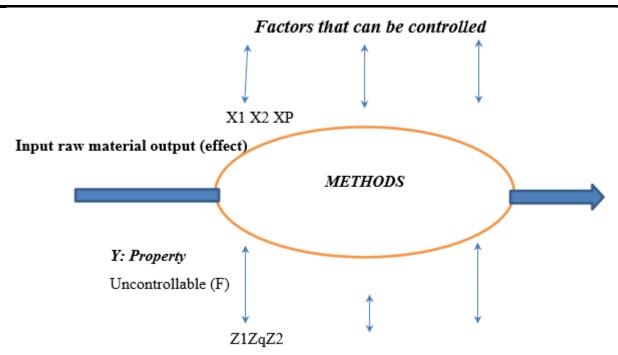


Fig.1: Source: Bertoline, (2012). Experimental flowchart. (Adapted by the authors, 2018).

It is necessary to consider some basic principles when planning an experiment in order to ensure that data is obtained in order to provide a correct analysis leading to valid conclusions regarding the problem under study, namely, the principle of repetition, the principle of casualization and local control principle (BORTOLINE, 2012).

This query or literature review possessedi intended to check the registered specifications of experimental designs that may or may not be usedof in a search, your goal is to present a theoretical and didactic knowledge of varieties of methods of a factorial design so you can help in the understanding and production of experimental design in order to optimize the work on an experimental scientific research.

#### II. METHOD

To identify articles on the subject was held search in the databases PubMed, ScienceDirect, Scopus and Sciello. The factorial experimental designs have based on the study of the influence of each variable in response study, covering in its experimental field the effects of influence between the variables of the systems, and the search strategy consisted in the use of key words in English: 1. Factorial design, 2. Experimental planning, 3. Multivariate analysis and 4 factorial experiment.The following filters have been added to search on ScienceDirect: only journals; title, abstract; key-words.

After consulting the databases and application of search strategy, studies repeated between different searches were identified. Inclusion criteria for articles were: original articles and research on factorial experimental design in common use in laboratories in different fields of research, including studies and preinstallation already installed and in Portuguese, English and Spanish.

The grouped articles were excluded in order: repeated irrelevant review, other publishing formats (notice, short communications, perspectives, letters), and other languages. In addition, manual searches were made in reference lists of review articles found with the predetermined keywords.

## III. RESULTS

After removal of the articles repeated between the different searches, the exclusion criteria were applied, as shown in Figure 2. Of the remaining 100 articles were retrieved 66 original research articles involving multivariate optimization in scientific papers in different areas of knowledge. Through manual search were recovered 2 more items.All articles related, after the exclusion criteria were related to the experimental design.

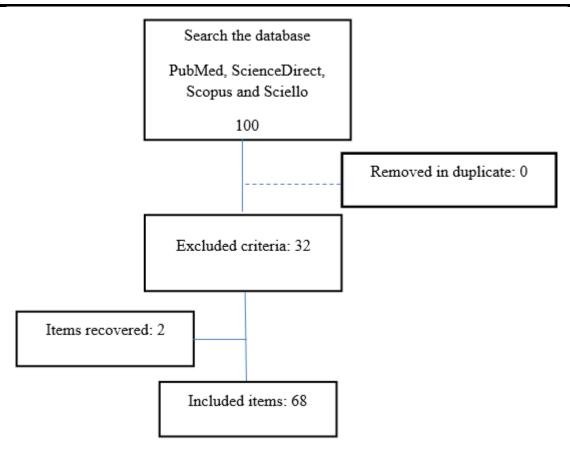


Fig.2: Flowchart of identification and selection of items. (Prepared by the authors, 2018).

## **3.1- FACTORIAL EXPERIMENTS**

The factorial experiment is a statistical tool that presents itself as a planned experiment, allowing you to observe the effects that several factors tend on a result. The factors from a variety of reactions allows to evaluate both a multitude of factors in an experiment (ANDERSON; WHITCOMB, 2010; WEBSTER, 2006; FREUND; WILSON; MOHR, 2010a, 2010b).

Factorial designs have the advantage of allowing the presumption of the effects of interaction between the various factors in addition to providing greater accuracy to estimate the effects of individual factors (DEY, 2011).

According to (PATIENCE, 2013), tools and techniques to plan, execute, analyze and apply results of experimental or development programs range from basic shapes such as trial and error, to detailed statistical plans that start with the selection of projects to identify factors as variables. According Patience (2013), the trial and error is present with the intuition of the researcher, namely his experience is effective when it begins to understand a problem. Patience (2013) states that despite the understanding, in most cases this strategy is inefficient compared to an experimental project, in which the factors are modified in defined increments at specific levels. Different, but with a didactic sense, LEITE LIMA et al., (2017) qualifies a variable according to its attributes. The experimental factorial design is effective in the study of two or more factors (Jaynes et al., 2013). The main effect may be defined as the change in the response due to a change in the factor level. The effect of interaction between the factors understands that the difference of a factor is not the same at all levels of the other factors. The main set of effects and interaction effects are the factor effects (WU & HAMADA, 2009).

ANDERSON; WHITCOMB, (2010) and KAREL D.VOHNOUT (2003) state that a factorial design can be defined as full or fractional. A full factorial experiment is an action of the researcher to measure responses vTheholiday combinations of factor levels. In full factorial experiments, the effects of the intervention components, or variables are independent, which makes it possible to estimate separately the main effect andtheirhigherorderinteractions (JAYNESet al., 2013).

In addition, the factorial experiment is able to efficiently estimate the main effects by the average of the other effects, the geometric growth of their samples while additionalvariables are added (ALLORE& MURPHY, 2008). The full factorial experiment can be the most efficient way to investigate a series of intervention components (COLLINS et al., 2009). In many cases, the main effects of five, six, or more factors can be studied with adequate power using the same sample size would be needed for a single factor (COLLINS et al., 2009). Full factorial experiments are possible even with cluster randomization (DZIAK et al., 2012).

However, there is a disadvantage of the full factorial design. According LEITE Lima et al., (2017) andNAHUM-SHANI; DZIAK: **COLLINS** (2017)thedisadvantageisTherelatedtoincrease in the number of experimental tests, as the factors or numbers expand. In this wayALASONATI et al., (2015) recommends reducing the maximum possible number of factors and the number of levels of each factor, otherwise the experimental design will be slightly manageable and very complex model. Using this reduction strategy in the number of variables it is possible a focus on key factors or variables (ANTONY, 2002).

When there is a large number of experimental factors you need to consider a fractional factorial design (Cochran & Cox, 1957). fractional factorial designs as well as offer many of the advantages of a full factorial design requires significantly smaller experimental conditions and is a variation of factorial designs, involving the use of a subset of the experimental conditions of a full factorial design, wisely chosen to preserve themainstatistical properties (NAHUM-SHANI DZIAK Collins, 2017).

In a fractional factorial design only a fraction or a subset of the full factorial experiment is selected and used (Allore & MURPHY, 2008). The fractional factorial experiments have been abundantly used in variousresearchareas(ZHOU, BALAKRISHNAN, &ZHANG, 2013).

The choice of which implement conditions has important consequences for the inference, this is done strategically, usually using software to allow an estimate of the effects of primary interest (DZIAK et al., 2012). The fraction is chosen by selecting one or more independent generators (FLEISS 1999) defining which variables are confusedwiththemaineffects (COCHRAN andCOX, 1957).

The confounded effects can not be estimated separately and distinguished from each other because the experimental levels of each matrix are identical in the experimental design (ALLORE&MURPHY, 2008). The interactions of more than two variables are considered harmlessly confused while the misconception about the main effects and two-way interactions need to be carefully considered (ALLORE& MURPHY, 2008). The procedure called blocking in factorial designs occurs when it is not possible to perform a large number of homogeneous plays together when this occurs the division into smaller executions is necessary, and is connected to confounding phenomenon (RAMAKRISHNAN, 2005).

To ensure that the effects of importance are not placed together is essential for the fractional factorial

design to be chosen a definition of relationship, which usually covers the choice of settings to ensure that only the words corresponding to factor the effects of higher order are included in relation (WOODS&LEWIS, 2017).

The resolution of a plan indicates the highest degree of interaction that is not confused with other interactions of the same order (COCHRAN&COX, 1957). This type of experiment can be useful when resources are limited or the numbers of experimental factors are larger, allowing the use of smaller numbers of tests (PATIENCE, 2013).

Furthermore, in clinical studies also using partialfactorial experiment. The partial factorial experiment is a study where the population is randomized. The study is a randomized controlled clinical trial use in medicine where certain variables that can be controlled, can seek to identify the relationship between these variables. The study seek to identify the relationship of the use of a drug and the improvement of patients. If you can control a determiner factor in at least a factor of interest and a subset of this population is randomized on one or more factors. The choice of how to restrict the random assignment has been determined by economic constraints, geographicalorclinics (ALLORE & MURPHY, 2008).

Second STEWART (2005) and LEITE LIMA et al., (2017) the factorial design is basically to conduct a survey of factors of a given experiment to analyze and evaluate the effects they exert against each other and on the final product. Still LEITE LIMA et al., (2017) this final product is the number of tests performed.

## 3.2 - Factorial designs 2K

Several authors have considered the factorial design as an important statistical tool capable of generating precise and accurate results, and enable the evaluation of multivariate way systems, optimizing all the variables that were part of the experimental system COSTA et al. (2006). Its application can be verified (Table 2) and is used in various projects developed in different areas of knowledge.

In general, this type of design is represented by k, where b represents the number of levels chosen and k the number of variables or factors (CUNICOet al., 2008). The levels are commonly called "high" and "low" or "absent" and "present," represented as follows: "+" and "-", "0" and "1", respectively (BORTOLINE, 2012).

This model is able to demonstrate the outstanding advantages of factorial design in a series of single factor studies. A wide range of research problems associated with interactions, main effects, among others, can be examined in terms of a linear combination of the average effects. It emphasizes that the designated linear comparison is the hypothesis of interest and reveals essential information that can not be obtained fromonlyfactorstudies (JAN &SHIEH, 2016).

Factorial Experiments two levels have the advantage of the fact does not always refer to a quantitative parameter can be used for qualitative questions, but also have pitfalls. They have only an approximation within experimental range; It does not contain replicated information; and being performed in just two levels are not abletoconsiderquadraticterms (BRERETON, 2018).

Because they are easy to use the factorial design of two levels are widely popular, moreover have simple calculations, but when the number of factors is considerable number of experiments to be performed becomes large, the front that makes it necessary to use other types of experiments (BRERETON, 2018).

# 3.3 - WORKS OF RESULTS WITH PLANNING FACTOR

Several authors have considered the factorial design as an important statistical tool capable of generating precise and accurate results, and enable the evaluation of multivariate way systems, optimizing all the variables that were part of the experimental system COSTA et al. (2006). Its application can be verified (Table 2) and is used in various projects developed in different areas of knowledge.

Methodology	Reference
	Moura et al. 2012
Randomized block design with factorial design	Silva et al. 2016
	Lisboa et al. 2016
	Cajazeira et al. 2018
	Gobbi et al. 2008
Completely randomized design with factorial design	Silva et al. 2018
	Chagas et al. 2013
	Tomala et al. 2014
	Peralta-Zamora et al. 2005
	Fandin and Duran 2004
	Cossa and Sirqueira
Full factorial design on two levels	Santos et al. 2018
	Lima and Gouveia 2012
	Maretti, E. et al. (2016)
	Antony, J. (2002)
	Costa et al. 2006
	FREUND; WILSON; MOHR, 2010a
	Neto et al. 2007
Simple factorial design	Webster, BJT (2006)
	Macagnan et al., 2017
	KATOVIC et al., 2001
	Jan, S. & Shieh, G., 2016
	Alasonati, E. et al. (2015)
	Zhou, Q. et al. (2013)
	Wang, PC (2007)
Fractional factorial two levels	Jaynes, J. et al., 2013
	Dziak, J. et al., 2012
	Besseris, G., 2013.
	Collins, L., et al., 2014
	Allore, H. & Murphy, T., 2008.
Factor planning with central points	Peloi et al. 2016
ractor praining with central points	Pereira Filho et al. 2002

 Table.2: Methodology From factorial arrangement in multivariate analysis

# International Journal of Advanced Engineering Research and Science (IJAERS) <u>https://dx.doi.org/10.22161/ijaers.5.6.28</u>

Factorial design in three levels	Bonaventure, RS et al. (2017)
Full factorial design (2 ^ k), individual experiments (2k), single	
factor (k + 1) and Fractional factorial design	Collins, L., et al., 2009

Investigated the work, according to the table mentioned above it was established the importance of using this model in the evaluation of statistical experimental data (Figure 3) to generate a precise answer and quality in various areas of knowledge, as described below.

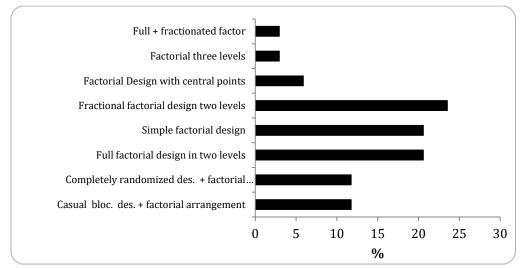


Fig.3: Use of factorial design in scientific papers.

To Cossa and Sirqueira (2009) factorial arrangement enabled himassess the multivariate way system and correlate all the variables related to the experimental system, theevaluate the use of tire compounds with polypropylene powder, in order to check the influence of input variables, represented by (Tire powder, dicumyl peroxide and bismaleimide) on the response variables, comprising (tensile, elongation and oil swell).

Similar, Cunico et al. (2008) found the practical application of experimental design in the statement of a study of relevant operational variables optimization, aimed at curing of methyl methacrylate (MMA) from the commercial acrylic glue B20 (BERKEL).

Since Chagas et al (2013) used a factorial arrangement 5 x 2 to evaluate the performance and pathophysiological of tambaquis responses (Colossoma macropomum) fed with feed supplemented with  $\beta$ -glucan corresponding to five different concentrations of immunostimulatory two sampling times.

For this same species, (TOMALA, 2014) with the objective of evaluating the consumption of oxygen according to body weight at different temperatures, we used a completely randomized design with a factorial arrangement 5x3x3, and (40, 60, 90, 140 and 250 g), and (21 26 to 31 ° C), respectively, with three replications. Associated with other statistical tool. ANOVA, the results

showed that oxygen consumption is related to temperature and inversely proportional to body weight.

Amaral et al (2017) used the experimental design for assessing the production of protease Aspergillus niger (SIS18) present in agroindustrial waste media, whey and cream residue. In his work took 22 type, ie adopted two levels +1 and -1 with two variables represented by the serum concentrations of glucose and Leite to the Leite and cream and residual glucose concentration for the second residue tested.

Also according to the authors, it could be seen through the results expressed in matrix encoded factorial design, that was maximum proteolytic activity in the assay two, ice cream and represented by residue glucose concentrations.

Already Arancibia et al (2010) used the factorial design in two stages, in order to optimize a procedure for determining zinc in seawater using voltammetric square wave stripping voltammetry (SWAdsV). In both cases, we used the planning on two levels, with four factors at first, being the variables analyzedpH, concentration of oxine (Cox), time (TADs) and potential (Eads) and the second adsorption optimum values of pH and Cox, by variance analysis showed that these two are the most significant parameters mentioned. The factorial analysis showed the best contractions are 6.0 to 25 mmol L-1, respectively.

Peloi (2016) to determine the antioxidant capacity and determination of total flavonoids in Verbena minutiflora also appealed to the factorial design. Initially used in the extraction methodwhere the variables for the determination of antioxidant capacity were pH, liquid extraction method, and extraction time. Subsequently the determination of total flavonoids evaluating variables: the concentration of hexamethylenetetramine, type of acid, acid volume, and heating time. According to their results the authors concluded to be the factorial design an important tool for extraction optimization of chemical components in natural products.

The effect of some variables on the enzymatic hydrolysis of sugarcane bagasse was investigated by Lima Gouveia (2012) using the factorial design at two levels with four variables 24, temperature, stirring (rpm), ethanol concentration and steps of adding enzymes, the latter being variable that showed significant result according to the authors.

A randomized block design in a factorial  $4 \times 2 + 6$  was adopted by Lisboa et al (2018). This type of design, beyond the principle of repetition and randomization, considers the principle of local control by establishing blocks. In his factorial design, the authors contemplated four cultivars of common bean intercropped with hybrid cultivars of castor, plus the cultivars mentioned in monoculture.

Together with other statistical tools, the aforementioned authors were able to identify which of the tested bean species showed better adaptation to the consortium with castor hybrids.

Maretti et al. (2016)used full factorial design of two levels, with no focal points and with three replicates for each level to assess the influence of new parameters pre-freezing of post SLNas (sets of solid lipid nanoparticles) and factors related to the process of prefreezing aiming to increase the inalabilidade SLNas filled with inhalable rifampicin. From the application of a DoE the author concluded that a quick freezing associated with a certain degree of dilution of the sample prior to the freezing step was able to refrain from the use of cryoprotectants, leading to extremely inhalable SLNas production showing income powder they require the use of excipients.

## IV. FINAL CONSIDERATIONS

Given the above it was found that the experimental design is a very important tool in the application of statistical analyzes in scientific papers, to allow a more complete analysis covering all the variables that make up the system, evaluating them simultaneously from the one fewer experiments compared with other univariate models. We found that many of the works for this article the most essential relative contribution resulting from the interaction of the researchers who make use of statistical methods has been to bring a better understanding of the logical questions that relate to the study. Further to this, we note that many of the scientific contributions are made during the early stages of the experimental design, which proceed to formal consideration of questions of a statistical project with data analysis.

Its application proved effective in the various areas of study, such as medicine, chemistry, agribusiness, veterinary, biotechnology and pharmaceuticals, reinforcing the finding of other authors of the force that this type of system has shown in recent years in various fields of knowledge. A large fragment of statistical literature focuses on the contribution that aleotorização and factorial experiments, and other formal statistics beliefs, contribute to the logic of the development of experimental programs.

A limited number of authors argue the methods that can obtain quantitative and qualitative information that is important to the logo of the period of project planning stages for a search. In examples we can mention that this important information can be obtained from construction diagrams with logic that should describe the proposal of the actions of experimental programs that the researcher want to study. Create exercises diagrams serve as a stimulus to manage evidence to support the needs of the shares, to remove logical inconsistencies in the experimental approach or to generate new ideas.

#### REFERENCES

- [1] ALASONATI, E., FABBRI, B., FETTIG, I., YARDIN, C., DEL CASTILLO BUSTO, M. E., RICHTER, J., FISICARO, P. (2015). Experimental design for TBT quantification by isotope dilution SPE-GC-ICP-MS under the European water framework directive. Talanta, 134, 576–586. doi.org/10.1016/j.talanta.2014.11.064
- [2] ALLORE, H. G., & MURPHY, T. E. (2008). An examination of effect estimation in factorial and standardly-tailored designs. Clinical trials, 5(2), 121-130. doi: 10.1177/1740774508089278
- [3] AMARAL, F. A. P. C.; FONSECA, T. C. S.; SALES, P. S. C.; SILVA, C. A. A. 2017.Produção de Protease por Aspergillus niger (SIS 18) em Meios Contendo Resíduos Agroindustriais Utilizando Planejamento Fatorial.ENGEVISTA, 19(5): 1320-1339
- [4] ANTONY, J. (2002). Training for design of experiments using a catapult. Quality and Reliability Engineering International, 18(1), 29–35. doi.org/10.1002/qre.444
- [5] ANDERSON, M. J.; WHITCOMB, P. J. Design of experiments. Kirk-Othmer Encyclopedia of

Chemical Technology, n. 1, p. 1–22, 2010.

- [6] ARANCIBIA, V.; ZÚÑIGA, M.; ZÚÑIGA, M. C.; SEGURAS, R.; ESTEBAN, M. 2010.Optimization of Experimental Parameters in the Determination of Zinc in Sea Water by Adsorptive Stripping Voltammetry.J. Braz. Chem. Soc., 21(2): 255-261
- [7] BESSERIS, G. J. (2013). A distribution-free multifactorial profiler for harvesting information from high-density screenings. PloS one, 8(8), e73275. doi: 10.1371/journal.pone.0073275
- [8] BRACARENSE, A. A. P.; TAKAHASHI, J. A. Modulation of antimicrobial metabolites production by the fungus Aspergillus parasiticus. Brazilian Journal of Microbiology, v. 45, n. 1, p. 313–321, 2014.
- [9] BISHOP, T.; PETERSEN, B.; TRAYSER, D. Another Look at the Statistician's Role in Experimental Planning and Design. The American Statistician, v. 36, n. 4, p. 387–389, 1982.
- [10] BOAVENTURA, R. S., YAMANAKA, K., OLIVEIRA, G. P., PINTO, E. R., & DE ANDRADE Maciel, M. B. (2017). Methodology for statistical analysis comparing the algorithms performance: Case of study in virtual environments in private cloud computing. IEEE Latin America Transactions, 15(2), 333–340.

https://doi.org/10.1109/TLA.2017.7854630

- [11] BORTOLINE, J. 2014. Estudos de experimentos fatoriais 2k aplicados em processo industrial. Dissertação (Mestrado em Estatística e Experimentação Agropecuária) – Universidade Federal de Lavras, Lavras-MG.
- [12] BOX, G., HUNTER, J. S., & HUNTER, W. G. (2005). Statistics for Experimenters: Design, Innovation, and Discovery.
- [13] BRERETON, R. G. (2018). Experimental design. In Chemometrics: Data Driven Extraction for Science, Second (Second Edi, pp. 11–99). JohnWiley & Sons Ltd.
- [14] CAJAZEIRA, J. P.; CORRÊA, M. C. M.; ALMEIDA, E. I. B.; QUEIROZ, R. F.; MESQUITAS, R. O. 2018. Growth and gas exchange in white pitaya under diferente concentrations of potassium and calcium1. Revista Ciência Agronômica, 49(1): 112-121
- [15] CHAGAS, E. C.; PILARSKI F.; SAKABE R.; MORAES, F. R. 2013.Desempenho produtivo e respostas fisiopatológicas de tambaquis alimentados com ração suplementada com β-glucano.Pesq.agropec. bras., Brasília, 48(8): 899-905

- [16] COCHRAN, W. G., & COX, G. M. (1957). Experimental designs, 2nd ed. Oxford, England: John Wiley & Sons.
- [17] COLLINS, L. M., DZIAK, J. J., KUGLER, K. C., & TRAIL, J. B. (2014). Factorial experiments: efficient tools for evaluation of intervention components. American journal of preventive medicine, 47(4), 498-504.doi: 10.1016/j.amepre.2014.06.021
- [18] COLLINS, L. M., DZIAK, J. J., & LI, R. (2009).
  Design of experiments with multiple independent variables: a resource management perspective on complete and reduced factorial designs.
  Psychological methods, 14(3), 202-224.doi: 10.1037/a0015826
- [19]COSSA, M. M.; SIRQUEIRA, A. S. 2009. Desenvolvimento de Elastômeros Termoplásticos Vulcanizados (TPV) a Base de Polipropileno com Resíduo de Pneu. I -Planejamento Fatorial de Experimentos.Polímeros: Ciência e Tecnologia, 19(3): 190-195
- [20] COSTA, L. M.; KOREN, M, G. A.; CASTRO, J. T.; SANTOS, W. P. C.; CARVALHO, E. V.; NOGUEIRA, A. R. A. 2006.Planejamento fatorial aplicado à digestão de amostras de feijão assistida por radiação micro-ondas. Quim. Nova, 29(1): 149-152
- [21] CUNICO, M. W. M.; CUNICO, M. M.; Miguel, O. G.; ZAWADZKI, S, F,; PERALTA-ZAMORA, P.; VOLPATO, N. 2008. Planejamento fatorial: uma ferramenta estatística valiosa para a definição de parâmetros experimentais empregados na pesquisa científica. Visão Acadêmica, Curitiba, 9(1)
- [22] CUNICO, M. W. M. W. M. et al. Factorial Desing: a Valuable Statistic Tool To Define Experimental Parameters Applied in Scientific Research. Visão Acadêmica, v. 9, n. 1, p. 23–32, 2008.
- [23] DEJAEGHER, B., & HEYDEN, Y. V. (2011).Experimental designs and their recent advances in set-up, data interpretation, and analytical applications.[Review].Journal of pharmaceutical and biomedical analysis, 56(2), 141-158.doi: 10.1016/j.jpba.2011.04.023
- [24] DEY, A. (2011). Factorial designs. Wiley Interdisciplinary Reviews: Computational Statistics, 3(6), 577–581.<u>https://doi.org/10.1002/wics.191</u>
- [25] DIAS-MAYER, F. FUMAGALLI-SCHETTERT, Giseane; SANTOS-SALBEGO, Dos Paulo Roberto; ISLONGO-CANABARRO, Nicholas; BALDO, Vanessa; MAZUTTI Antônio, Marcio.; FOLETTO, Edson, Luiz .; HOFFMANN, Ronaldo. Using factorial design to increase the efficiency on a smallscale ethanol distillation. Revista Tecnica de la

Facultad de Ingenieria Universidad del Zulia, v. 40, n. 2, p. 48–56, 2017.

- [26] DZIAK, J. J., NAHUM-SHANI, I., & COLLINS, L. M. (2012). Multilevel factorial experiments for developing behavioral interventions: power, sample size, and resource considerations.
- [27] FARDIM, P. & DURAN, N. 2004.Retention of Cellulose, Xylan and Lignin in Kraft Pulping of Eucalyptus Studied by Multivariate Data Analysis: Influences on Physicochemical and Mechanical Properties of Pulp. J. Braz. Chem. Soc., 15(4): 514-522
- [28] FISHER, R. A., & BENNETT, J. H. (1990).Statistical methods, experimental design, and scientific inference. Oxford: Oxford University Press.
- [29] FLEISS, J. L. (1999). Factorial Experiments The Design and Analysis of Clinical Experiments.
- [30] FREUND, R. J.; WILSON, W. J.; MOHR, D. L. Factorial Experiments. In: Statistical Methods. Third Edit ed. [s.l: s.n.]. p. 473–520.
- [31] FREUND, R. J.; WILSON, W. J.; MOHR, D. L. Design of Experiments. In: Statistical Methods. Third Edit ed. [s.l: s.n.]. p. 521–576.
- [32] FREUND, R. J.; WILSON, W. J.; MOHR, D. L. Design of Experiments. [s.l: s.n.].
- [33] GOBBIL, K. F.; GARCIA, R.; VENTRELLA, M. C.; NETO, A. F. G.; PEREIRA, O. G. Leaf tissues degradation of signalgrass hay pretreated with urea and submitted to in vitro digestion. 2008. R. Bras. Zootec., 37(5): 802-809.
- [34] ILZARBE, L., ÁLVAREZ, M. J., VILES, E., & TANCO, M. (2008). Practical applications of design of experiments in the field of engineering: a bibliographical review. Quality and Reliability Engineering International, 24(4), 417-428. doi: doi:10.1002/qre.909
- [35] JAN, S. L., & SHIEH, G. (2016). A systematic approach to designing statistically powerful heteroscedastic 2 x 2 factorial studies while minimizing financial costs. BMC medical research methodology.16(1), 114.doi: 10.1186/s12874-016-0214-3
- [36] JAYNES, J., DING, X., XU, H., WONG, W. K., & HO, C. M. (2013). Application of fractional factorial designs to study drug combinations.
- [37] KAREL D.VOHNOUT. Experimental tests for a system analysis problem. In: mathematical modeling for system Analysis in Agricultural Research. tucson, Arizona - EUA: [s.n.]. p. 344–385.
- [38] KENETT, R. S., & STEINBERG, D. M. (2014). Factorial Experiments. Wiley StatsRef: Statistics Reference Online, 1–6. doi.org/10.1016/B978-0-12-

374970-3.00009-3

- [39] KNIGHT, R., JANSSON, J., FIELD, D., FIERER, N., DESAI, N., FUHRMAN, J. A., GILBERT, J. A. (2012). Unlocking the potential of metagenomics through replicated experimental design.
- [40] LABUTO, G.; SILVA, L. R.; DOMINGUEZ, H. T. S.; CARRILHO, E. N. V. M.;GONÇALVES, N. S.; RODRIGUES, C. A. 2017. Efficient degradation of solid yeast biomass from ethanol industry by Fenton and UV-Fenton processes applying multivariate analysis. Rev. Ambient. Água, 12(6).
- [41] LEARDI, R. Experimental Design. 1. ed. [s.l.] Copyright © 2013 Elsevier B.V. All rights reserved., 2013. v. 28
- [42] LEITE Lima, Claudiany, S. BARROS, Danielle C.; REIS, Davi, T.; DENIS. S. Passos; NAIANE G. Silva.; PEDRO.G.B.Bonfim.; MATTJE, Vanessa, M.; SHEIDT Gessiel, Newton e PORTELLA Augustus Caeser Franke. Factorial Planning and Response Surface for the Definition of Experimental Parameters in Scientific Research, a Review. International Journal of Current Rrsearch, v. 9, n. 7, 2017.
- [43] LIMA, D. A.; GOUVEIA, E. R. 2012. Aplicação do planejamento fatorial 24 na hidrólise enzimática do bagaço de cana-de-açúcar. Revista Brasileira de Produtos Agroindustriais, Campina Grande, 14(3): 275-280.
- [44] LISBOA, C. F.; SILVA, D. D. A. S.; TEIXEIRA, I. R.; SILVA, A. G.; MOTA, J. H. 2018. Agronomic characteristics of common bean and castor bean hybrids in intercropping and monocropping. Revista Brasileira de Engenharia Agrícola e Ambiental, 22(3): 200-2015
- [45] MARETTI, E., RUSTICHELLI, C., ROMAGNOLI, M., BALDUCCI, A. G., BUTTINI, F., Sacchetti, F., IANNUCCELLI, V. (2016). Solid Lipid Nanoparticle assemblies (SLNas) for an anti-TB inhalation treatment—A Design of Experiments approach to investigate the influence of pre-freezing conditions on the powder respirability. International Journal of Pharmaceutics, 511(1), 669–679. doi.org/10.1016/j.ijpharm.2016.07.062
- [46] MONTGOMERY, D. C. (2006). Design and Analysis of Experiments: John Wiley \& Sons. Oberg, A. L., & Vitek, O. (2009).Statistical design of quantitative mass spectrometry-based proteomic experiments.[Review].Journal of proteome research, 8(5), 2144-2156.doi: 10.1021/pr8010099
- [47] MOURA, W. M.; CASALI, V. W.; CRUZ, C. D.; LIMAS, P. C. 1999. Divergência genética em linhagens de pimentão em relação à eficiência

nutricional de fósforo1. Pesq. agropec. Bras., Brasília, 34(2): 217-224.

- [48] NAHUM-SHANI, I., Dziak, J. J., & COLLINS, L. M. (2017). Multilevel Factorial Designs With Experiment-Induced Clustering. Psychological Methods. doi.org/10.1037/met0000128
- [49] NETO, F. B.; GOMES, E. G.; NUNES, G. H. S.; OLIVEIRA, E. Q. 2007. Desempenho de sistemas consorciados de cenoura e alface avaliados através de métodos uni e multivariados.Hortic. bras., 25(4).
- [50] PATIENCE, G. S. Experimental Planning. In: Experimental Methods and Instrumentation for Chemical Engineers. 1. ed. [s.l: s.n.]. p. 67–102.
- [51] PELOI, K.E.1; BOVO, F.; MESSIAS-REASON, I. J. 2; PEREZ, E. 2016. Utilização de planejamento fatorial para a determinação da capacidade antioxidante e doseamento de flavonoides totais em Verbena minutiflora Briq. ex Moldenke (gervai). Rev. Bras. Pl. Med., Campinas, 18(1): 1-8.
- [52] PERALTA-ZAMORA, P.; MORAIS, J. L.; NAGATA, N. 2005. Por que otimização multivariada? Eng. Sanit. Ambient.10 (2): 106-110
- [53] PEREIRA-FILHO, E. R.; POPPI, R. J.; ARRUDA, M. A. Z. 2002. Emprego de planejamento fatorial para a otimização das temperaturas de pirólise e atomização de al, cd, mo e pb por ETAAS.Quim. Nova, 25(2): 246-253
- [54] POLITIS, S. N., Colombo, P., Colombo, G., & REKKAS, D. M. (2017). Design of experiments (DoE) in pharmaceutical development. Drug Development and Industrial Pharmacy, 43(6), 889– 901. doi.org/10.1080/03639045.2017.1291672
- [55] RAMAKRISHNAN, V. (2005). Factorial Experiments. In Encyclopedia of Biostatistics (pp. 1–5). John Wiley & Sons, Ltd. doi.org/10.1002/0470011815.b2a16023
- [56] SETHURAMIAH, A.; KUMAR, R. Statistics and Experimental Design in Perspective. In: Modeling of Chemical Wear. [s.l: s.n.]. p. 129–159.
- [57] SANTOS, G. S.; Silva, L. O. B.; SILVA, A. F.; SANTOS, J.; SILVA, E. G. P.; SANTOS, W. N. L.; Analytical Strategies for Determination and Environmental Impact Assessment of Inorganic Antimony Species in Natural Waters Using Hydride Generation Atomic Fluorescence Spectrometry (HG AFS). 2018. J. Braz. Chem. Soc., 29(1): 185-190
- [58] SILVA, M. I. L.; NASCIMENTO,W. G.;RODRIGUES, C. R.; VASCONCELOS, M. A. S.; SOARES, G. S. C. Silicon as an attenuator of salt stress in Brachiaria brizantha 'MG5'1.2018.Revista Ciência Agronômica, 49(1): 130-140
- [59] SILVA, R. A.; SOUZA, U. O.; SANTOS, L. G.; MELO, N. C.; VASCOCELOS, R. C. 2016.

Características agronômicas de cultivares de milho verde submetidas a doses de Ribumin. Revista de Ciências Agrárias, 39(3): 395-403

- [60] STEWART, F. P. (2005). Fractional Factorial Designs. In Encyclopedia of Biostatistics (pp. 1–7).
   John Wiley & Sons, Ltd. doi.org/10.1002/0470011815.b2a16025
- [61] TANCO, M., Costa, N., & VILES, E. (2009). Experimental design selection : guidelines for practitioners. International Journal of Productivity and Quality Management, 4(3), 283–302.
- [62] TOMALÁ, D.; CHAVARRIA, J.; ESCOBAR, B. E. A. 2014.Evaluación de la tasa de consumo de oxígeno de Colossoma macropomum en relación al peso corporal y temperatura del agua.Lat. Am. J. Aquat. Res., 42(5): 971-979
- [63] THOMKE, S. H. (1998). Managing Experimentation in the Design of New Products. Management Science, 44(6), 743-762. doi: 10.1287/mnsc.44.6.743
- [64] WU, J., & HAMADA, M. (2009). Experiments: Planning, Analysis, and Optimization.
  WANG, P. C. (2007). Planning experiments when some specified interactions are investigated.
  Computational Statistics and Data Analysis, 51(9), 4143–4151. doi.org/10.1016/j.csda.2007.02.004
- [65] WEBSTER, B. J. T. (2006). Factorial Experiments, an example. In Encyclopedia of Statistical Sciences (pp. 1–6).
- [66] WOODS, D.C., & LEWIS, S.M. (2017) Design of experiments for screening. In Handbook of Uncertainty Quantification. 1143-1185 doi.org/10.1007/978-3-319-12385-1
- [67] ZHOU, Q., BALAKRISHNAN, N., & ZHANG, R. (2013). Analysing Categorical Data Log-linear analysis. The Canadian Journal of Statistics, 41(3), 540–555. doi.org/10.1002/cjs