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A systematic and critical review of two decades' application of response surface methodology in biological wastewater treatment processes

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ABSTRACT

Response surface methodology (RSM) has been applied to design experiments, analyze operative parameters, produce models, and optimize operational conditions in water and wastewater treatment processes. Although various aspects of RSM application in physicochemical wastewater treatment processes have been scrutinized, the biological processes are considered more efficient methods for wastewater treatment. Thus, evaluation of RSM application in biological processes would be useful research to reduce costs and number of experiments in biological treatment processes as well as to achieve its milestones in future studies. In this study, a thorough systematic and critical review evaluated two decades of RSM application in conventional biological treatment processes, including aerobic, anaerobic, anoxic, combined, and lagoon processes, to clarify its limitations and suggest crucial enhancements for future studies.

Keywords: Response surface methodology; Biological wastewater treatment; Aerobic; Anaerobic; Anoxic; Lagoons

1. Introduction

1.1. Literature review

The growing world population is increasingly producing industrial, domestic and agricultural wastewater containing various kinds of pollutants, which have induced adverse effects associated with aquatic environment pollution and human health [1]. To safely release into the environment, wastewaters are treated through physical unit operation as well as chemical and biological processes. Amongst them, the biological processes have been considered for wastewater treatment due to their reliability, eco-friendly nature, and lower costs [1,2]. The major biological processes are typically divided into aerobic, anoxic, anaerobic, and combined aerobic/anaerobic/anoxic (A^2/O) processes, which are shown in Table 1 [3]. As a conventional aerobic suspended growth process, the activated sludge (AS) has been widely applied for treating different types of wastewater, as many research groups have attempted to improve the efficiency of this technology [2,4–9]. Other aerobic processes have also been implemented in many researches to meet more stringent discharge standards over the years, which entail membrane bioreactor (MBR) [10–15], moving bed bioreactor (MBBR) [16,17], packed-bed reactors [18], rotating biological contactors (RBC) [1], and trickling filters (TF) [19].

Anoxic processes (suspended and attached growth) are generally implemented to remove nitrogen from wastewater, which is known as the denitrification process [20]. Anaerobic processes such as upflow anaerobic sludge blanket (UASB) [21], anaerobic packed and fluidized bed [22], anammox process [23], and anaerobic digestion [24] have also been applied due to their general advantages, namely, less energy required, less biological sludge production,

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and less nutrients required. Also, a potential energy source (methane), smaller reactor volume, elimination of off-gas air pollution, and potential for lower carbon footprint are considered as additional merits of the anaerobic processes [3]. In addition, to achieve efficient and economical solutions of wastewater treatment, the different conditions of aerobic, anoxic, and anaerobic have been integrated [25–39].

For the treatment process evaluation, a number of parameters should be taken into account in order to analyze the effective parameters and their interactions on process' performance [40]. The traditional approach, which is termed one-factor-at-a-time, analyzes one parameter by keeping other parameters at a constant level; and for optimization of a multivariable process, one factor at a time is considered. This approach does not deliberate the interplays between the chosen parameters, and it needs a large number of experiments to evaluate all chosen parameters that make it a time-consuming and high costing method [40,41]. In a systematic procedure, the design of experiment (DOE) is applied to evaluate the relationships between the effective parameters and outputs (responses), which obtain the maximum amount of information in the smallest number of conducted experiments. The choice of a DOE depends on the objectives of the experiment and the number of factors to be investigated and reduces the number of experiments required to be conducted, lead to the decrease of the energy and material consumption and the laboratory works reduction [41]. Amongst various methods of DOE, response surface methodology (RSM) has been most commonly considered as an appropriate means to model and analyze the processes [41,42]. RSM involves main impacts and interplays, and it could additionally present quadratic or cubic terms for curvature' explanation [42,43].

1.2. Research gap

RSM as a convenient tool to design experiments, to produce models, and to analyze the effects of the parameters has been applied in more than 80 papers of five major biological wastewater treatment methods, including, aerobic, anaerobic, anoxic, combined, and lagoon processes in the last two decades. Thus, systematic evaluation of RSM application in these processes would be a useful topic in the area of RSM application. Application of RSM in physicochemical treatment processes has been reviewed by Karimifard and Alavi Moghaddam [44] for dye removal from wastewater and Nair's research group for water/wastewater treatment processes [40]. However, considering the literature, there has been no thorough review paper that sums up the application of RSM in biological processes to achieve its milestones in future studies. Hence, the main aim of this study is to systematically and critically investigate two decades of RSM application in conventional biological processes, to clarify its limitations in such processes, and, most importantly, to suggest crucial enhancements for future studies.

2. Tools and methodology

2.1. Tool: RSM as a statistical model

DOE is a systematic method of solving engineering problems that employ principles and techniques to produce accurately valid outcomes after collecting data with minimum time and costs [45]. Considering the National Institute of Standards and Technology (NIST) guidelines, five basic steps of a DOE analysis are characterized as follows [43]:

- Look precisely at the data and get a holistic perspective and construct various graphs.
- Produce a theoretical model.
- Generate a model from the data via regression methods in steps and/or *p*-value significance of parameter.
- Verify the model assumptions via appropriate procedures such as analysis of variance (ANOVA).
- Apply the outcomes to address the experimental purposes, clarify significant parameters, and find optimum conditions.

Choosing a DOE depends highly on the experiments' objectives and the number of selected parameters. According to the experimental purpose, types of designs fall into several categories, such as RSM objective, comparative objective, screening objective, mixture objective, regression model objective [43]. The RSM is the most important purpose, in which the experiments are designed to approximate interactions as well as quadratic impacts so as to produce a figure of the response surface [46].

The origin of RSM was introduced by Box and Wilson [47], in which the RSM employing in chemical processes as described. This study had a reflective effect on industrial applications of experimental design, and consequently, it motivated many researchers [48]. After Box and Wilson's primary idea for RSM, the fundamentals of RSM were discussed in many papers and textbooks [49–56]. The most comprehensive discussion is provided in a book [49] written by a group of chemists, engineers, and statisticians. During the 1950s, classical designs of RSM were divided into two extensive categories, including Box–Wilson central composite designs (CCDs) and Box–Behnken designs (BBDs) [43], which are described as follows:

2.1.1. Box–Wilson CCDs

A Box–Wilson CCDs is an embedded factorial or fractional–factorial design, which has center points with an increased set of star points to approximate the curvature. For each factor, if the distance of center point from a factorial point is ±1, the distance from a star point is $|\alpha| > 1$. The α value is calculated by the number of factors $\alpha = (2^k)^{1/4}$; k is the number of factors [57–59]. There are three types of CCDs, including central composite circumscribed [CCC, and in some cases the central composite rotational (CCR)], central composite inscribed (CCI), and central composite face-centered (CCF) [41,43]. In Table 2, different types of CCDs (for two factors) are described.

2.1.2. Box–Behnken designs

The BBDs have no embedded factorial or fractional–factorial design that makes it an independent quadratic design. This design considers the midpoints of edges of the space and the center point for combinations. The BBDs require three levels of each factor and are of rotatability [41,43]. In comparison with CCDs, these designs are of restricted ability for orthogonal blocking [60,61].

2.2. Methodology

2.2.1. Searching methodology

A summarized description of the applied searching methodology for this paper is presented in Fig. 1. Through Scopus, a thorough search was performed in February 2020, the world's largest database for peer-reviewed literature with a wide range of disciplines to address the research query and ensure the systematic quest. The Scopus content comes from over 5,000 publishers worldwide that must be reviewed and selected by an independent Content Selection and Advisory Board, which provides reliable information and data for researchers [62].

In this research, a systematic review of the published literature on the application of RSM in biological wastewater treatment was performed using qualitative data analysis guidelines. Based on the authors' experiences, four initial keywords, including "response," "surface," "method," and "wastewater" were determined and resulted in over 2500 published research works. In the next step, the abstracts of the papers were precisely evaluated in terms of "Subject Area," "Document Type," and "Language," and consequently, the irrelevant published works were eliminated according to the exact purpose of the present study. This study focused on the papers that were published in international scientific journals and excluded "Book chapters," "Conference papers," "Reviews and Textbooks". The language of papers was also restricted to "English". In addition, the works, which applied the RSM to the activated sludge models, were ignored due to their different approaches. Finally, amongst more than 2,500 papers, 84 papers were chosen to conduct the current review.

2.2.2. Analysis methodology

According to the main aim of this study, two approaches, including "informative" and "critical," were considered. In the "informative" approach, distribution trends of the related papers by major biological processes, year of publication, journals, and correspondence authors' country/nationality were analyzed. The final 84 documents were carefully re-assessed to avoid the possible inaccuracies of Scopus' analysis section. In the "critical" approach, as illustrated in Fig. 2, application of RSM and applied software for five major processes were analyzed according to the leading textbook of wastewater treatment [3]. In addition,

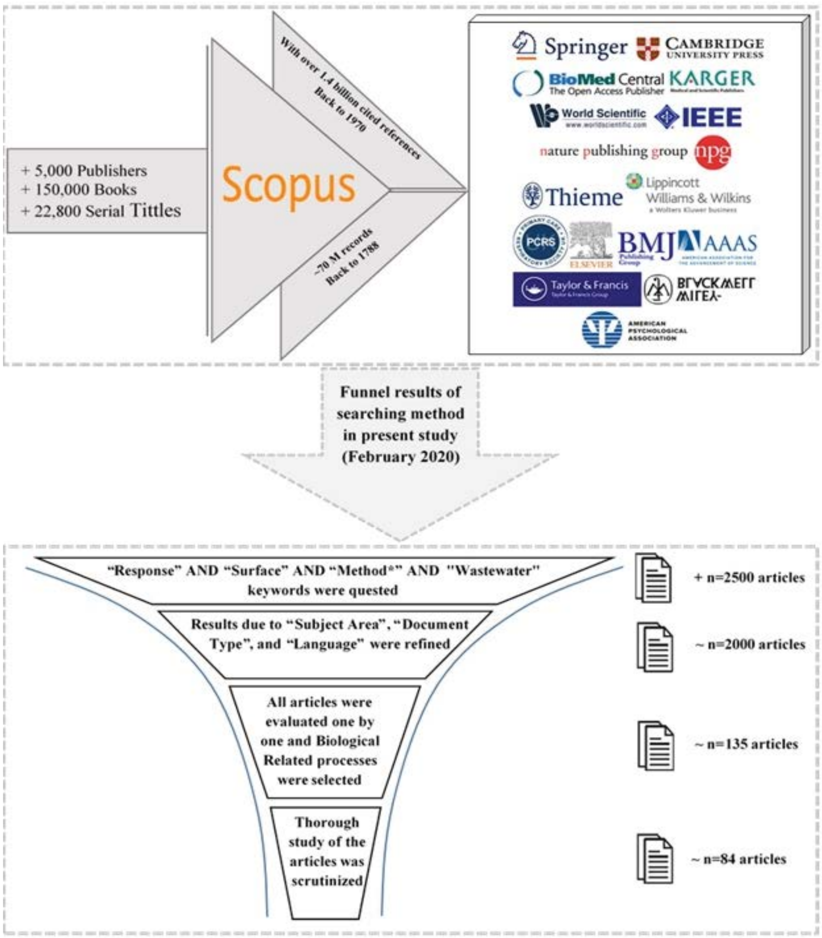


Fig. 1. Searching methodology in the present study.

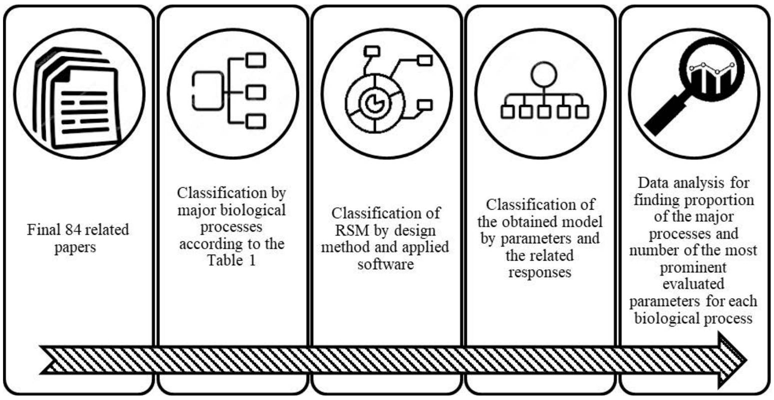


Fig. 2. Critical analysis procedure used in the present study.

in each paper, the applied parameters and the related responses of the models were classified, and finally, the most prominent evaluated parameters were found for each biological process.

3. Results and discussion

3.1. Distribution trends of results

In this study, distribution trends of the 84 selected papers were investigated according to three perspectives, including major biological processes, year of publication and journals, and correspondence authors' country/nationality, which are described as follows:

3.1.1. Classification by major biological processes

According to the aim of this study and due to the main biological processes for wastewater treatment (Table 1), every 84 papers were thoroughly reviewed to classify the applied biological processes (Fig. A1). The results showed that the most application of RSM in biological processes was in the aerobic (50% of 84 papers) and the combined aerobic/anaerobic/anoxic processes (33% of 84 papers). In aerobic processes, the AS, MBBR, MBR, RBC, and TF were identified to be precisely analyzed in terms of RSM application.

3.1.2. Classification by year of publication and journals

Distribution of the 84 selected papers by year of publication, the related journals as well as their quartiles rank is presented in Fig. 3. As is shown in Fig. 3, the RSM application in biological wastewater treatment has initiated since 2009 and has been significantly increased in the last two decades. The most published papers were in 2014 and 2017 (35% of 84 papers). In the previous two decades, about 47 journals contributed to publishing 84 papers, and the top five journals published papers are listed as follows:

- Desalination and Water Treatment: 13 papers,
- Bioresource Technology: 7 papers,
- Journal of Environmental Chemical Engineering: 4 papers,
- Journal of Environmental Management: 4 papers,
- Process Safety and Environmental Protection: 4 papers.

More than 70% of the journals are of Quartiles rank of Q1 and Q2.

Classification by correspondence authors' country: Distribution of the papers by the correspondence authors' country is presented in Fig. 4. As is shown, the largest number of studies were conducted in Iran with 36 publications (about 43%); Furthermore, China, Malaysia, and India, altogether, published more than 30 papers in this field. As a result, the application of RSM in biological wastewater treatment processes has been mainly used by developing countries more than that of developed countries; it may be related to the limited funds allocated to scientific researches in the developing countries. In addition, the list of top universities/research centers and a number of their published papers is provided as below:

- Razi University, Iran (30 publications)
- Kermanshah University of Medical Sciences, Iran (12 publications)
- Universiti Teknologi Malaysia, Malaysia (6 publications)
- Hamedan University of Medical Sciences (5 publications)
- Ryerson University, Canada; Hangzhou Normal University, China; Babol Noshirvani University of Technology, Iran; and Universiti Sains Malaysia, Malaysia (all with 4 publications)

3.2. Critical procedure of RSM application in biological treatment processes

In this section, the 84 classified papers have been precisely investigated according to the main biological processes for wastewater treatment (Table 1). Hence, the selected papers classified in separate tables with emphasis on detailed information, including the following items:

- Year of publication
- RSM: including design method and software
- Treatment process: including the type of wastewater and method of treatment
- Model: including parameters and responses

3.2.1. Aerobic processes

An aerobic process occurs in the presence of free dissolved oxygen, which is conventionally applied in biological

Table 1
Main biological processes for wastewater treatment [3]

Type	Suspended/attached	Common name
Aerobic processes	Suspended growth	Activated sludge process (AS) Aerated lagoons Aerobic digestion Membrane bioreactor (MBR) Nitritation process
	Attached growth	Biological aerated process Moving bed bioreactor (MBBR) Packed-bed reactors Rotating biological contactors (RBC) Trickling filters
	Hybrid processes	Trickling filters/activated sludge Integrated fixed film activated sludge (IFAS)
Anoxic processes	Suspended growth	Suspended growth denitrification
	Attached growth	Attached growth denitrification filter
Anaerobic processes	Suspended growth	Anaerobic contact processes Anaerobic digestion Anammox process
	Attached growth	Anaerobic packed and fluidized bed
	Sludge blanket	Upflow anaerobic sludge blanket (UASB)
	Hybrid	Upflow sludge blanket/attached growth
Combined aerobic, anoxic, and anaerobic processes	Suspended growth	Single or multi stage process, various proprietary processes
	Hybrid	Single or multi stage suspended growth processes with fixed film media
Lagoon processes	–	–

wastewater treatment [3]. As is shown in Table 3, all papers related to the aerobic process, including AS, MBBR, MBR, RBC, and TF with the application of RSM (42 out of 84 papers), have been published between 2009 to 2019. Also, more than 85% of the papers (36 out of 42 papers) applied CCD of RSM, and more than 75% (33 out of 42 papers) used Design-Expert software for the design of their experiments. In case of the wastewater type, 42 studies used real wastewaters including hospital [63,64], pulp and paper [65], municipal [18,66–69], dairy [2,70], industrial [71,72], leachate [73], textile dying [74–76], slaughterhouse [77], woodchips [78], and oil refinery [79] and the rest of the studies applied synthetic wastewater [80–98].

According to Table 3, evaluation of effective parameters and their interactions through RSM are presented for aerobic processes. The main important parameters were initial pollutant concentration, hydraulic retention time (HRT), biomass concentration, aeration rate, and solids retention time (SRT). Also, about 75% of the papers had more than one response. For more details, some of these papers were described as follows:

Khondabi et al. [79] applied the CCD method of RSM to evaluate the RBC process for the treatment of real oil refinery wastewater. Three independent variables with three levels, including temperature (35°C, 40°C, and 45°C), rotational speed (2, 8, and 14 rpm), and disc submergence (30%, 40%, and 50%) were investigated to find their effects on chemical oxygen demand (COD) and phenol removals. The optimum amount of removals achieved using RSM were 94.25% and 81.09% for phenol and COD, respectively.

Karami et al. [63] used the RSM method for the AS process so as to evaluate two independent parameters' effect (biomass concentration and HRT) on COD removal efficiency, turbidity reduction and sludge volume index (SVI) for treating real hospital wastewater. The CCD method was applied to design the experiments with 3 levels for each independent factor, and the experiments were implemented in two levels: with sonication and without sonication. In addition, the simultaneous optimum conditions to meet all the responses' limitations (COD removal > 90%, effluent turbidity < 3 NTU, and SVI < 90 mL/g) were achieved MLSS = 7,000 mg/L and HRT = 5 h with sonication.

Qaderi et al. [90] applied the RSM design for treating synthetic wastewater using the MBBR process and three independent variables, including retention time, influent total petroleum hydrocarbon (TPH), and media filling ratio, as well as interactions between variables, were evaluated on TPH removal efficiency. The highest removal efficiency 97% was obtained in retention time = 23 h, wastewater feed concentration = 164.78 m/L, and media filling ratio = 45%.

Shim et al. [92] implemented the BBD method of RSM in the MBR process to determine the detachment efficiency of bio-cakes for treating synthetic wastewater. For this purpose, the influence of aeration rate, bead number, and bead diameter with three levels (high = +1, middle = 0, low = –1)

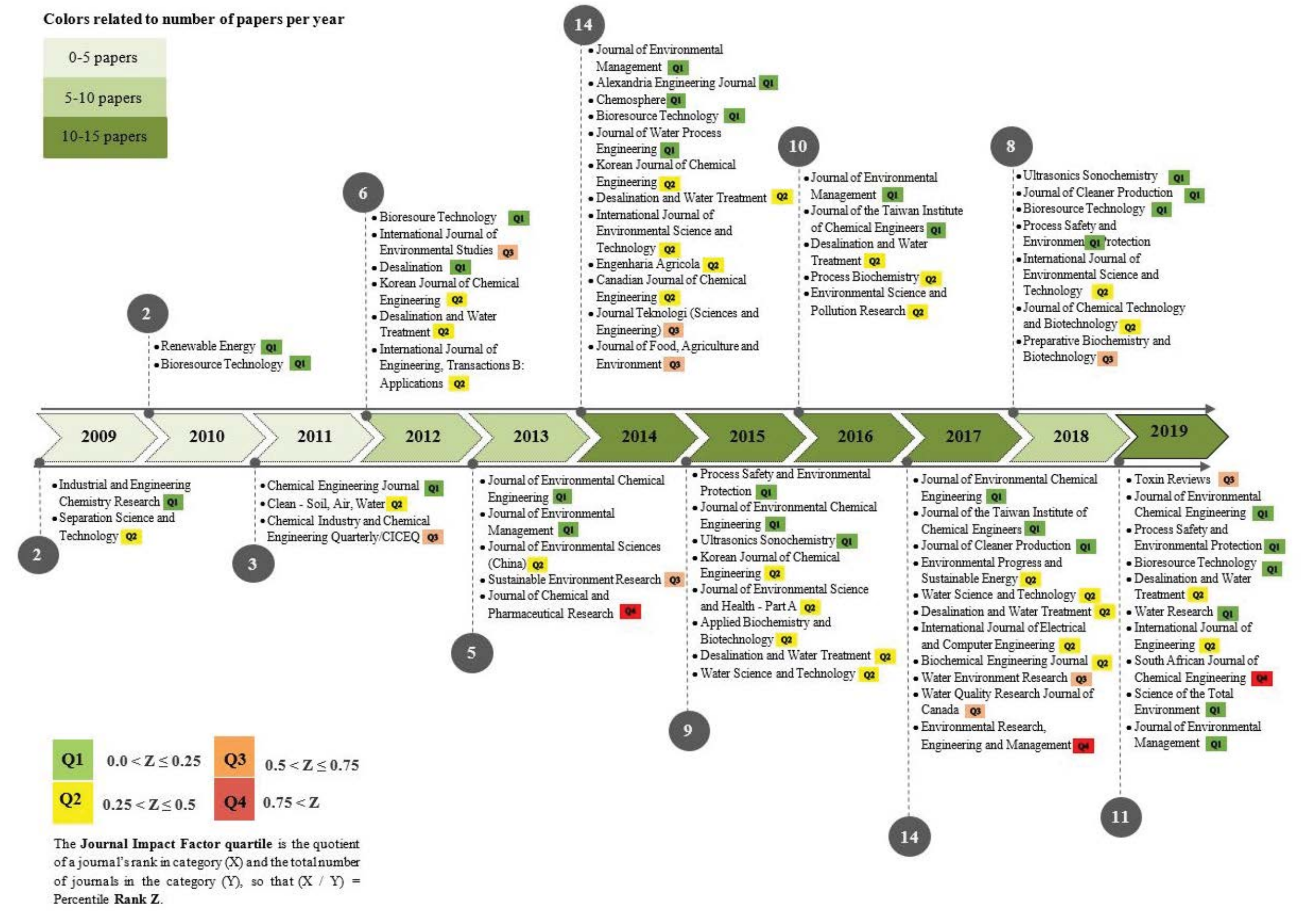


Fig. 3. Distribution of papers by year of publication, the related journals as well as their quartiles rank.

was investigated. The optimal conditions were also achieved using MINITAB optimizer with 0.057 m^3/h, 140 beads, and 3.8 mm for aeration rate, bead number, and bead diameter, respectively.

3.2.2. Anaerobic processes

An anaerobic process takes place in the absence of free dissolved oxygen which produces biomass, methane, and carbon dioxide gas as final products [3]. As is shown in Table 4, all papers related to anaerobic process including UASB, anaerobic contact processes, and anaerobic digestion with the application of RSM (8 out of 84 papers) were published between 2010 to 2019. More than 60% of the papers applied CCD and Design-Expert software for the design of their experiments. Both real (pulp and paper industry [103], biodiesel [104], municipal [105], swine [105], and brewery [106]) and synthetic wastewater [21,107–109] were used in the 8 anaerobic processes. Amongst the 8 papers, two of them were described in the following paragraph to clarify more details about RSM application in an anaerobic process.

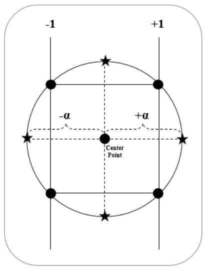
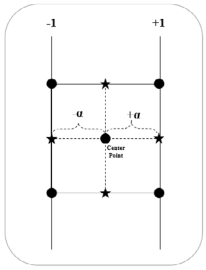
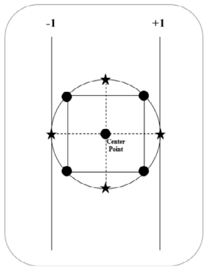
For instance, Najib et al. [21] evaluated the UASB to treat both real and synthetic wastewater; using the CCF method of RSM, the effect of independent parameters, including pH, initial SO_4^{2-}, COD/SO_4^{2-} ratio, and $COD_{ethanol}/COD_{total}$ ratio, have been investigated on sulfate removal efficiency. Also, the sulfate removal was achieved 97.87% at optimum conditions of 7.19, 2,153.15 mg/L, 2.72, and 1 for pH, initial SO_4^{2-}, COD/SO_4^{2-} ratio, and $COD_{ethanol}/COD_{total}$ ratio, respectively.

Boonsawang et al. [104] employed BBD to evaluate the anaerobic contact process for treating biodiesel wastewater. Three independent variables with three levels, including pH, organic loading rate (OLR) (g COD/L d), and HRT (h) were investigated for two acidogenic and methanogenic reactors, separately. COD removal (%) and biogas production (L/d) were considered as the responses for the methanogenic reactor, and COD removal, long chain fatty acid (LCFA) consumption, and volatile fatty acid (VFA) production were three responses for the acidogenic reactor.

3.2.3. Anoxic processes

According to the results, only one study (out of 84 papers) implemented the RSM method in an anoxic process. Zhang et al. [20] applied the attached growth denitrification filter to treat real industrial wastewater. They investigated the HRT effects and influent (COD and NO_3–N) concentrations on NO_3 removal efficiency and improved the parameters' conditions to predict the optimum responses. Also, to scrutinize the response surface model additional tests excluding axial, center, and factorial points were done in other two solid-phase denitrification biofilters in the same operating

Table 2
Various types of CCDs by two factors example [41,43]

Type of CCDs	Abbreviation	Description	Pictorial representation
Circumscribed	CCC	It is the original form of the CCD. The star points have same distance α from the center. For all factors, the star points create new extremes for the low and high settings. This design requires 5 levels for each factor.	
Face-centered	CCF	The star points are at the center of each face of the factorial space (α = ±1). This design requires 3 levels of each factor.	
Inscribed	CCI	If the factor settings have specified limits, the star points were designed using the factor settings and generates a factorial or fractional factorial design within those limits. (CCI design is a scaled down of CCC design with each factor level of the CCC design divided by α to produce the CCI design). This design requires 5 levels of each factor.	

In some cases, the central composite rotational (CCR) is applied rather than CCC.

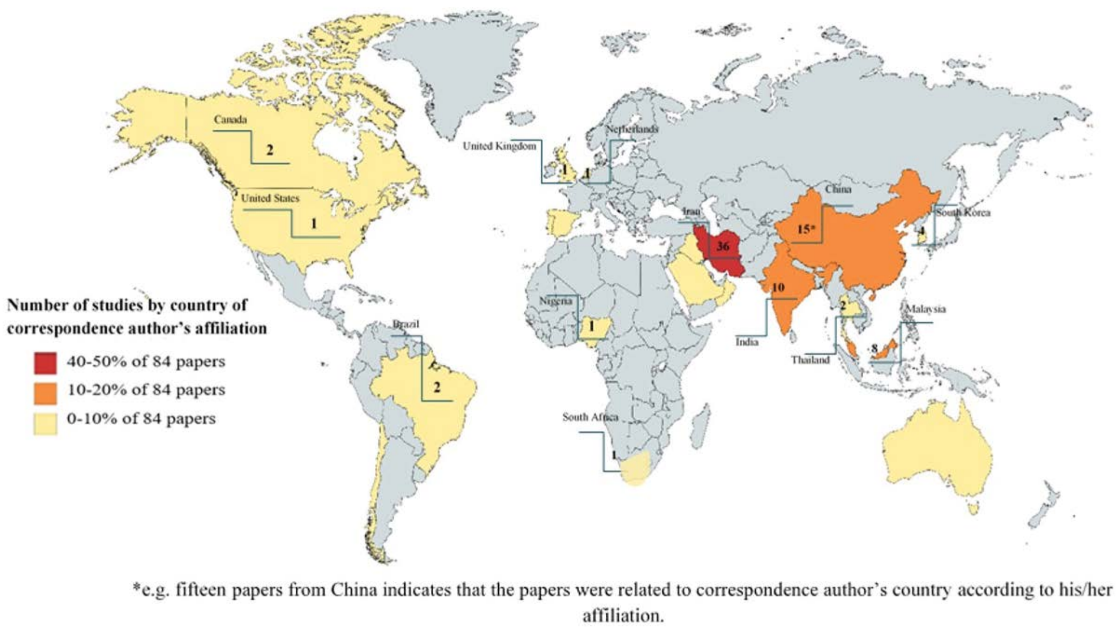


Fig. 4. Distribution of contribution in the 84 selected papers by the country of correspondence authors.

Table 3
Application of RSM in aerobic processes

Year	RSM		Biological treatment process		Model		References
	Design method	Software	Wastewater type	Method	Parameters	Responses	
2019	CCD	Design-Expert v7.0.0	Woodchips wastewater	AS	Initial COD (mg/L) Cycle time (h) Biomass concentration (MLSS) (mg/L)	COD reduction (%) Turbidity removal (NTU)	[78]
		Design-Expert v11.0.0	Synthetic wastewater	MBBR	Initial pH HRT (day) Type of carrier	COD removal (%)	[93]
		Design-Expert v10.0.2.0	Synthetic wastewater	MBBR	HRT (h) NO_3 recycle ratio	TN removal efficiency (%) TP removal efficiency (%) Volumetric OLR (kgCOD/m^3 d) Surface OLR (g COD/m^2 d) Volumetric NLR (kg NH_4^+–N/m^3 d) Surface NLR (g NH_4^+–N/m^2 d)	[82]
		Design-Expert v7.0.0	Oil refinery wastewater	RBC	Temperature (°C) Rotational speed (rpm) Disc submergence (%)	Phenol removal (%) COD removal (%)	[79]
		Design-Expert v8.0.0	Synthetic inorganic wastewater	TF	HRT (day) NH_4^+–N concentration (mg/L)	NH_4^+–N removal efficiency (%) Removal rate (kg NH_4^+–N/m^3 d)	[94]
		Design-Expert v8.0.0	Synthetic inorganic wastewater	TF	HRT (h) COD/N ratio	NH_4^+–N removal efficiency (%) COD removal (%) TN removal efficiency (%)	[84]
	CCF	–	Dairy wastewater	AS	HRT Air flow rate	Carbon removal (%) Nutrients removal (%)	[70]
		Design-Expert v7.0.0	Hospital wastewater	AS	Biomass concentration (MLSS) (mg/L) HRT (h)	COD removal (%) Turbidity (NTU) SVI (mg/L)	[63]
		Design-Expert v7	Pulp and paper wastewater	AS	Initial COD (mg/L) Cycle time (h) Biomass concentration (MLSS) (mg/L)	Color removal (%) COD reduction (%) SVI	[65]
2018	CCD	Design-Expert v10.0.6	Synthetic wastewater	MBBR	Retention time (h) Influent total petroleum hydrocarbon (TPH) concentration (mg/L) Media filling ratio (%)	TPH removal (%)	[90]
		Design-Expert v10	Synthetic wastewater	MBBR	HRT (h) NH_4^+/$NH_4^+NO_3$ ratio	Soluble chemical oxygen demand (SCOD) removal (%) TN removal (%) Effluent N–NO_3^- (mg/L) Effluent turbidity (NTU)	[88]

2017	BBD	Design-Expert v9	Municipal wastewater	MBBR	Flow rate (L/h) Nitrate concentration (mg/L) Phosphate concentration (mg/L)	Nitrate removal (%) Phosphate removal (%)	[18]
		Design-Expert v6.0.7	Palm oil mill effluent and municipal wastewater	AS	Aeration (L/min) Aeration time (h) MWW/POME ratio (%)	Turbidity removal (%)	[67]
		Design-Expert v7	Synthetic wastewater	AS	Biomass concentration (MLSS) (mg/L) Carbon source	COD removal (%) Effluent total suspended solids (TSS) (mg/L) SVI (mL/g)	[95]
		–	Textile dyeing industry wastewater	AS	Temperature (°C) Sorbent dosage (g/L) Biomass support (%, v/v)	Decolorization (%) COD reduction (%) SVI (mL/g)	[75]
	CCD	MINITAB v16.1 and other statistical calculations using Microsoft Excel	Domestic sewage, raw petroleum refinery wastewater, and pre-treated petroleum refinery effluent	AS	Inlet phenol (mg/L) Inlet ammonia (mg N/L) Inlet phosphate (mg P/L)	Effluent phenol (mg/L)	[99]
		Design-Expert v10.0.0.3	Synthetic wastewater	MBBR	Carrier filling ratio (%) Aeration rate (m^3/h) Reactor run time (day)	COD removal (%) Biochemical oxygen demand (BOD) removal (%) Total Kjeldahl nitrogen (TKN) removal (%) TP removal (%) Turbidity removal (%)	[83]
	CCF	Design-Expert v8.0	Synthetic dyeing wastewater	AS	Zn concentration (mg/L) Co concentration (mg/L) Mo concentration (mg/L)	COD removal (%)	[97]
	BBD	Design-Expert v6.0.4	Domestic wastewater	AS	Temperature (°C) Time (day)	Total chemical oxygen demand (TCOD) removal (%) TP removal (%)	[69]

(continued)

Table 3 Continued

Year	RSM		Biological treatment process		Model		References
	Design method	Software	Wastewater type	Method	Parameters	Responses	
2016	CCD	Design-Expert v10.0.0.3	Actual slaughterhouse wastewater	AS	Influent total organic carbon (TOC, mg/L) Flow rate (mL/min) pH Inlet H_2O_2 (mg/L)	TOC removal (%) TN removal (%) H_2O_2 residual (%) CH_4 production (%)	[77]
		Design-Expert v9.0.0.4	Real municipal wastewater	MBBR	Bio-carrier filling rate (%) Aeration rate (m^3/h) Reactor run time (day)	BOD removal (%) COD removal (%) TKN removal (%)	[66]
	CCF	Design-Expert v8.1	Synthetic wastewater	AS	Biomass concentration (MLSS1) (mg/L) Biomass concentration (MLSS2) (mg/L) Ozone concentration was controlled as feed-gas and off-gas	Effluent COD (mg/L)	[80]
		Design-Expert v6.0.7	Landfill leachate and household wastewater	AS	Aeration rate (L/min) Contact time (h) Leachate-to-wastewater ratio (%)	Fe removal (%) Mn removal (%) Ni removal (%) Cd removal (%)	[73]
	CCD	Design-Expert v7.0.0	Synthetic wastewater	AS	RSM stage: Input COD (mg/L) pH Exchange ratio Cycle time (h) Aeration rate (L/min)	RSM stage: COD removal (%) TSS (mg/L) SVI (mL/g)	[96]
2015	CCD	Design-Expert v8.0.4	Mixed printing and dyeing wastewater	AS	HRT (h) pH Sludge loading rate (SLR) (kg COD/(kg MLSS d))	COD removal (%) Terephthalic acid (TA) removal (%)	[74]
		Design-Expert v6.0	Hospital wastewater	MBBR	Aeration time (h) Mixing (min) Biomass concentration (MLSS) (mg/L)	COD removal (%) BOD removal (%) TKN removal (%) TN removal (%)	[64]
	CCF	Design-Expert v7	Dairy wastewater	AS	Numerical: Aeration time (h) Biomass concentration (MLSS) (mg/L) COD (mg/L) Categorical: Sonication	COD removal (%) Final turbidity (NTU) Settling velocity (m/h) SVI (mL/g)	[2]

2014	CCD	Design-Expert	Landfill leachate and domestic wastewater	AS	Aeration rate (L/min) Contact time (h) Leachate to wastewater ratio (%)	COD removal (%) Color removal (%) Ammoniacal nitrogen (NH_3–N) removal (%) Phenols removal (%)	[100]
		MINITAB v16 and Design-Expert v7.0	Synthetic wastewater	AS	Sodium bicarbonate/ammonium chloride ratio Air flow rate (L/min) Reaction time (h)	Ammonium removal (%)	[86]
	CCF	Design-Expert v8.0	Industrial wastewater (Synthetic antibiotic wastewater)	AS	Biomass concentration (MLVSS) (mg/L) COD (mg/L)	Directly: COD removal (%) Effluent TSS (mg/L) Effluent turbidity (NTU) SVI (mL/g) Indirectly: U (g $COD_{removal}$/g VSS d)	[91]
	BBD	MATLAB used for optimization	Textile dye wastewater	AS	Air flow rate (LPH L/h) SRT (day) Cycle period (h)	Decolorization (%) COD reduction (%) SVI (mL/g)	[76]
		MINITAB	Synthetic wastewater	MBR	Bead diameter (mm) Bead number Aeration rate (m^3/h)	Detachment efficiency of bio-cakes (%)	[92]
2013	CCD	Design-Expert v7.0	Industrial estate wastewater	AS	Biomass concentration (MLVSS) (mg/L) Number of working aerators (NA)	COD removal (%) BOD removal (%) TSS removal (%) TP removal (%) Effluent N–NO_3	[72]
	CCF	Design-Expert v8	Synthetic wastewater	MBBR & Aeration lagoon	Phenol Concentration (mg/L) m-cresol concentration (mg/L) Residence time (h)	Phenolics removal (%)	[87]
2012	CCD	Design-Expert v6.0.6	Industrial estate wastewater	AS	Aeration time (h) Biomass concentration (MLVSS) (mg/L)	TCOD removal (%) rbCOD removal (%) BOD removal (%) TN removal (%) TP removal (%) SVI (mL/g) Settling velocity (m/h) Effluent turbidity (NTU)	[71]

(continued)

Table 3 Continued

Year	RSM		Biological treatment process		Model		References
	Design method	Software	Wastewater type	Method	Parameters	Responses	
2012	CCF	Design-Expert v7.01	Dairy and synthetic wastewater	AS	Biomass concentration (MLSS) (mg/L) COD/N/P ratio Aeration time (min/h) Cycling time (h)	COD removal (%) TKN removal (%) N–NO_3^- removal (%) Effluent N–NO_3^- (mg/L) Effluent TN (mg/L)	[81]
		Design-Expert	Synthetic milk wastewater	AS	COD influent (mg/L) HRT (h) Recycle ratio	TCOD removal (%) SVI (mL/g) specific substrate utilization rate (*U*) (g COD_{rem}/g VSS d)	[101]
	BBD	MATLAB 7.6	Synthetic wastewater	MBR & MBBR	SRT (day) HRT (h) Temperature (°C) Aeration rate (m^3/h)	Soluble microbial products (SMP) production (mg/L)	[85]
		MINITAB	Domestic wastewater	MBBR	Aeration flow rate (101 kPa m^3/h) Aeration time (min) Aeration position (cm)	COD removal (%) NH_3–N removal (%) TN removal (%) TP removal (%)	[68]
2011	CCF	Design-Expert	Municipal wastewater	AS	Initial COD (mg/L) Rotational velocity (rpm) Temperature (°C) Retention time (h)	COD removal (%) Particulate COD reduction (mg/L) Sulfate reduction (mg S–SO_4/L) Total sulfide generation (mg S/L) $TS_{generated}$/$TCOD_{removed}$ (mg $S_{produced}$/g COD_{rem}) Sulfide generated/sulfate reduced (mg $S_{produced}$/S–$SO_{4\ reduced}$) $Sulfate_{reduced}$/$TCOD_{removed}$ (mg S–$SO_{4reduced}$/g $COD_{removed}$) (H_2S (aq)/TS) H_2S (%) H_2S emitted (mg S/L) Alkalinity produced (mg $CaCO_3$/L) Final pH	[102]
		Design-Expert v6.0.7	Synthetic dairy wastewater	MBBR	COD influent (mg/L) Biomass concentration (mg/L) Aeration time (h)	COD removal (%) SVI (mL/g)	[98]
2009	CCD	MINITAB	Sewage wastewater treatment plant	AS	OLR (COD) (mg/L d) SRT (day) DO (mg/L) Calcium ion (mM)	SVI (mL/g) Turbidity (NTU) COD outlet (mg/L) COD removal rate (mg/L d) SS outlet (mg/L)	[89]

Table 4
Application of RSM in anaerobic processes

Year	RSM		Biological treatment process		Model		References
	Design method	Software	Wastewater type	Method	Parameters	Responses	
2019	CCD	Design-Expert v10.0.0	Synthetic sugar industry wastewater	UASB	Temperature (°C) C/N ratio (mg TOC/mg N) pH	COD removal (%) Biogas production (L/d)	[106]
2017	CCF	Design-Expert v7.0.0	Real and synthetic wastewater	UASB	Initial SO_4^{2-} (mg/L) COD/SO_4^{2-} ratio $COD_{ethanol}/COD_{total}$ ratio	Sulfate removal (%)	[21]
2016	BBD	Design-Expert v8	Bagasse effluent from pulp and paper industry	UASB	Influent COD (mg/L) HRT (h) Temperature (°C)	COD removal (%) COD removal rate (mg/L h) Biogas production (L/d)	[103]
2015	BBD	Essential Regression and Experimental Design for Chemists and Engineers Version 5.0c running on Microsoft Excel 1998	Biodiesel wastewater	Anaerobic contact process	pH HRT (h) OLR (g COD/(L d))	COD removal (%) Biogas production (L/d) VFA production LCFA consumption	[104]
2014	CCD	Design-Expert v8	–	Anammox/UASB	Fe^{3+} (mg/L) Cu^{2+} (mg/L) Ni^{2+} (mg/L)	Specific anaerobic ammonium (SAA)	[108]
		Design-Expert v8.0.6.1	Synthetic wastewater	UASB/attached growth	Influent substrate concentration (TN_{inf}) (mg/L) HRT (h) Upflow velocity (m/h)	Nitrogen removal (%) (NRE) Nitrogen removal rate (NRR) (kg m^3/d)	[109]
2010	CCD	–	Municipal wastewater and swine wastewater	Anaerobic digestion	Temperature (°C) HRT (day)	Total volatile fatty acids (g/L)	[105]
	BBD	MINITAB v15	Brewery wastewater	UASB	Temperature (°C) pH Brewery wastewater concentration (BWC) (g/L)	H_2 yield (mL H_2/g COD) H_2 maximum production rate (mL/h)	[106]

conditions of the CCD experiment; relative error between 3.7 and 6.7% confirmed the agreeable relation of responses with the predicted values.

3.2.4. Combined aerobic/anaerobic/anoxic processes

In order to achieve efficient and cost-effective treatment of wastewater, different conditions of aerobic, anoxic, and anaerobic are combined with each other [3]. As is shown in Table 5, all papers related to combined processes with the application of RSM (28 out of 84 papers) were studied between 2009 to 2019. Also, more than 75% of the papers (24 out of 84 papers) implemented CCD of RSM and Design-Expert software. For more details of the application of RSM in combined processes, five papers were elaborated on as follows.

Srisuwun et al. [110] investigated an anaerobic sequencing batch reactors (SBR) system for treating synthetic wastewater through the CCD method, during which effluent of reactive red 159 (mg/L), decolorization (%), and decolorization rate (g/L h) were evaluated. At optimum conditions of independent variables (reactive red 159 concentration = 6,500 mg/L, SRT = 20 d, and HRT = 8 d) decolorization efficiency was achieved 97.68% ± 0.74%.

Mansouri and Zinatizadeh [111] used the CCF method to evaluate a combined process of two feeding regimes in AS reactors including batch fed (SBR) with intermittent aeration and continuous fed (up-flow aerobic/anoxic sludge fixed film (UAASFF) bioreactor) for P and N removal in synthetic wastewater. Three effective parameters entailing retention time (HRT), aeration time, and COD:N:P ratio were opted for analyzing purposes. As a result, the UAASFF bioreactor, as opposed to the SBR, was confirmed to be a proper bioreactor with higher nutrients removal efficiency as well as at lower HRT.

Wang et al. [23] used the BBD method in an alternating aeration MBR to investigate simultaneous partial-nitrification, denitrification, and anammox process for total nitrogen (TN) and COD removal from synthetic wastewater. The independent variables of influent carbon to nitrogen (C/N) ratio, anaerobic period (min), and airflow (L/min) were evaluated through RSM so as to reach optimal conditions (C/N = 0.46, aerobic/anaerobic = 2.6 min, and airflow = 0.50 L/min). Finally, optimum TN removal and COD removal were achieved at 92.4% and 98.1%, respectively.

Akhbari et al. [112] evaluated independent parameters' effects (Total HRT, recirculation ratio: from aerobic to anoxic zone, COD/N/P, and speed of rotating disks) on COD removal, TN removal, effluent NO_3 and phosphorus removal through the CCD design method in a combined AS and RBC system for treating synthetic wastewater. In order to optimize the responses, TCOD removal, effluent NO_3^-, and TN and total phosphorus (TP) removal were limited to >90%, <10 mg/L, >70%, and >74%, respectively. At an optimum point with HRT = 18.3 h, rotating disks speed = 10 rpm, COD/N/P = 12, and recirculation ratio = 2.5 of the aerobic unit, COD, TN, and TP removals were obtained 62%, 22%, and 57%, respectively.

Kim et al. [113] applied multiple RSM to model and optimize the selected variables dissolved oxygen (DO set point, wasted-sludge, and internal recycling) in a standard anaerobic/anoxic/oxic (A^2O) process for biological wastewater. Two responses of N removal and P removal were simultaneously optimized through maximized desirability function, consequently, at optimal operating conditions of 1, 27.5 g/m^{3,} and 3,850 g/m^3 for DO set point, wasted-sludge, and internal recycling, respectively, the high removal efficiency of N = 78% and P = 80% were obtained.

3.2.5. Lagoon processes

As is shown in Table 6, all papers related to the lagoon process with the application of RSM (5 out of 84 papers) were published between 2013 to 2019. Also, CCD of RSM and Design-Expert software was applied for the design of the lagoon process experiments in most of the studies. For instance, Qaderi et al. [137] scrutinized the phenol removal in serial stabilization ponds with synthetic wastewater. Two independent variables of temperature and initial phenol concentration were used in RSM experimental design. According to the applied model, optimum phenol removal was obtained 42.1% at optimal conditions of 14.20°C and 109.58 mg/L for temperature and initial phenol concentration, respectively.

3.2.6. Overall discussion

RSM is an appropriate tool to design and optimize various biological processes. In the current study, 84 papers of two decades have been comprehensively scrutinized to reveal the detailed application of RSM in biological treatment processes. Using RSM in aerobic, anaerobic, anoxic, combined and lagoon processes has been evaluated by numerous research groups. However, 84 studies are all the researches implemented in the application of RSM in biological treatment processes, while there is still a great potential for more studies. In addition, the biological processes that applied RSM could enhance their approach in a different stage of modeling and optimization. According to Fig. 5, the percentage of the 84 studies is categorized into five main biological treatment methods. As is shown, 50% of the papers studied aerobic processes that applied RSM, in which 36 types of independent parameters were considered in RSM design. Also, about 33% of the articles were related to combined A^2O processes with 31 types of independent parameters. Also, Table 7 illustrates the most prominent evaluated parameters of RSM for each biological process used among the 84 analyzed papers. According to Table 7, the important parameters used in the majority of RSM models were classified separately for each biological process, which could reveal the significant effective parameters in biological processes. As is shown in Table 7, initial pollutant concentration (mg/L) was the most significant parameter in all aerobic, anaerobic, anoxic, combined, and lagoon processes. For instance, this parameter was applied 18 times in aerobic processes (12 times in AS process, 5 times in MBBR process, and 1 in TF process). In addition, being applied 8 times anaerobic and 12 times of the combined methods reveal the importance of the initial pollutant concentration in the RSM design of biological methods. The second significant parameter was the HRT (h or day), which the most used was in aerobic and combined processes. The next important parameters were biomass concentration (mg/L), airflow rate (L/min), SRT (day), temperature (°C), and

Table 5
Application of RSM in combined aerobic/anaerobic/anoxic processes

Year	RSM		Biological treatment process		Model		References
	Design method	Software	Wastewater type	Method	Parameters	Responses	
2019	CCD	Design-Expert v8.0	Synthetic domestic wastewater	Integrated anoxic/oxic biological aerated filter	Influent distribution flow ratio of the first step (%) Influent distribution flow ratio of the second and the third steps	TN removal (%)	[114]
	CCF	Design-Expert v11.0	–	Partial nitritation (PN)/anaerobic ammonium oxidation (Anammox) in SBR	Ratio of the amount of influent injected at each aerobic phase to the amount of influent injected at each sub-cycle Amount of feed distribution at each aerobic phase	Effluent NH_4^+ concentration Effluent N concentration TN removal (%) Nitrogen removal rate (kg/m^3 d)	[115]
2018	CCD	Design-Expert v7	Yoghurt wastewater	Hybrid expanded granular sludge bed and fixed-bed bioreactor	COD (mg/L) HRT (h) COD/nitrogen ratio (COD/N)	COD removal (%) Final COD (mg/L) OLR (kg/m^3 d) Biogas production rate (BPR) (mL/h)	[116]
		Design-Expert v6.0.10	Synthetic wastewater	Anaerobic SBR	HRT (day) SRT (day) Dye concentration (mg/L)	Dye effluent (mg/L) Decolorization (%) Decolorization rate (g/L/h)	[110]
	CCD	Design-Expert v9.0.6	Synthetic wastewater	Anaerobic/anoxic/Oxic (A^2O) (MBBR) integrated system	Nitrate recycle ratio HRT (h) Influent COD (mg/L)	COD removal (%) TN removal (%) TP removal (%) SVI (mL/g)	[117]
		–	Industrial wastewater contain phenol compounds	Biofilter and AS (BF/AS)	DO (mg/L) HRT (h) Biomass concentration (MLSS) (mg/L) Glucose concentration (mg/L)	Phenol removal (%)	[118]

(continued)

Table 5 Continued

Year	RSM		Biological treatment process		Model		References
	Design method	Software	Wastewater type	Method	Parameters	Responses	
2017	CCF	Design-Expert v6.0.7	Synthetic wastewater	Two bench scale AS (upflow aerobic/anoxic sludge fixed film (UAASFF) bioreactor	HRT (h) COD:N:P ratio Aeration time for UAASFF (min/h) Cycle time Aeration time for SBR (min/h)	SCOD removal (%) TN removal (%) TKN removal (%) Effluent nitrate (mg/L) Phosphorous removal (%)	[111]
	BBD	Design-Expert v9.0.6.2	Actual slaughterhouse wastewater	Anaerobic baffled reactor (ABR) followed by an aerobic AS	Flow rate (mL/min) pH Influent TOC (mg/L)	TOC removal (%) TN removal (%) TSS residual (mg/L) Biogas yield (mL/min)	[119]
	CCF	Design-Expert v6.0.6	Real industrial wastewater	Upflow aerobic/anoxic sequential bioreactor (UAASB) with an alternate aeration	HRT (h) Aeration time (min)	TCOD removal (%) NO_3–N production (mg/L) BOD removal (%) COD removal (%) TP removal (%)	[120]
2016	CCF	Design-Expert v7.0	Real milk processing wastewater	Upflow anaerobic/anoxic/aerobic sludge bed (UAAASB) bioreactor under two different mixing conditions	HRT (h) Aeration time mode Biomass concentration (MLSS) (mg/L) F/M ratio	SCOD removal (%) TN removal (%) TKN removal (%) Denitrification rate (g/L d) Effluent nitrate (mg/L) Effluent nitrite (mg/L) TP removal (%) Effluent turbidity (NTU) SVI (mL/g) Height of sludge (m) DO (mg/L)	[121]
	BBD	Design-Expert	Synthetic wastewater	Simultaneous partial nitrification, Anammox and denitrification (SNAD) in an intermittent aeration (MBR)	Influent C/N ratio Anaerobic period (min) Air flow (L/min)	TN removal (%) COD removal (%)	[23]
		Design-Expert v7.0	Milk processing wastewater (dairy wastewater)	Upflow anaerobic/aerobic/anoxic bioreactor	HRT (h) Aeration mode Biomass concentration (MLSS) (mg/L)	COD removal (%) TN removal (%) TP removal (%)	[122]

2015	CCD	Design-Expert v8.1	Swine wastewater	Two-step fed SBR	First/second volumetric feeding ratio First anaerobic/aerobic (an/oxic) time ratio Second an/oxic time ratio	TN removal (%) Ammonium nitrogen (NH_4–N) removal (%) TP removal (%) Dissolved phosphorous removal (%) COD removal (%) BOD removal (%)	[123]
	BBD	Design-Expert v7	High-strength composite leachate	Hybrid expanded granular sludge bed and fixed bed reactor	COD (mg/L) HRT (h) COD/nitrogen ratio	COD removal (%) BPR (mL/h)	[124]
		Design-Expert v8.0.1	Municipal wastewater	Hybrid-upflow sludge blanket filtration bioreactor	COD (mg/L) Biomass concentration (mg/L) HRT_{total} (h)	COD removal (%)	[125]
		Design-Expert v8.0.6	Synthetic and real wastewater	A²O process	SRT (day) HRT (h) Initial tetracycline (μg/L)	Tetracycline removal (TC) (%)	[126]
		–	Synthetic wastewater	Gas–Liquid–Solid bioreactor	Air flow rate (L/m) Biofilm carrier (g/L) Carbon source (mg/L) Temperature (°C) pH	Nitrate removal (%)	[127]
2014	CCD	–	Synthetic wastewater	AS and Nitrification/denitrification	Ca concentration (mg/L) Phosphorus concentration (mg/L) pH	Removed Ca (mg/L) Removed phosphorus (mg/L)	[128]
		Design-Expert v6.0.11	Soy sauce wastewater	Alternating anaerobic/aerobic SBR	Circulation rate (L/h) Operation time (day)	COD removal (%) SVI (mL/g) MLVSS/MLSS (%)	[129]
		Design-Expert	Synthetic wastewater	Aerobic/anoxic sequence batch reactor (SBR)	Cycle time (h) Aeration time (min/h)	TCOD removal (%) TN removal (%) Phosphorus removal (%) TKN removal (%) Effluent nitrate (mg/L)	[130]

(continued)

Table 5 Continued

Year	RSM		Biological treatment process		Model		References
	Design method	Software	Wastewater type	Method	Parameters	Responses	
2013		–	Cattle slaughterhouse wastewater	Nitrification/denitrification processes in SBR	Initial concentration of ammonia-nitrogen (mg/L) Air flow rate (L/min $L_{reactor}$)	Ammonia-nitrogen conversion to NO_3 (%) NO_2^- accumulation (%) TN removal (%)	[131]
	CCR (CCC)	–	Slaughterhouse effluents	SBR conventional process by nitrification and denitrification	Cycle time (h) Carbon:nitrogen ratio	Ammonia nitrogen removal (%) Nitrite removal (%) Nitrate removal (%) Total inorganic nitrogen removal (%)	[132]
		MINITAB v13.32 and Design-Expert v7.0	Synthetic dyeing wastewater	Bio-granules in anaerobic–aerobic SBR	Substrate concentration (mg/L) Riboflavin concentration (μM)	COD removal (%) Color removal (%)	[133]
	CCR (CCC)	Design-Expert	Palm oil mill effluent	Integrated anaerobic-aerobic bioreactor (IAAB)	OLR (g COD/L d) Biomass concentration (MLVSS) in anaerobic compartments (mg/L) Biomass concentration (MLVSS) in aerobic compartments (mg/L)	COD removal in aerobic and anaerobic (%) BOD removal in aerobic and anaerobic (%) TSS removal in aerobic and anaerobic (%) Methane yield (L CH_4/g COD d) Effluent pH Effluent VFA (mg/L) Effluent TA (mg/L) Final COD (mg/L) Final BOD (mg/L) Final TSS (mg/L)	[134]
	CCF	Design-Expert v6.0.10	Recycled paper wastewater	Granular activated carbon sequencing batch biofilm reactor (GAC-SBBR)	HRT (day) Aeration rate (m^3/min) Influent feed concentration (mg COD/L)	COD removal (%) Ammoniacal nitrogen (NH_3–N) removal (%) 2,4-dichlorophenol (2,4-DCP) removal (%)	[135]

2012	CCD	Design-Expert v7.0	Industrial estate wastewater	Upflow sludge bed reactor (USBR) and SBR	HRT (h) Aeration time (min/h) Aeration mode	TCOD removal (%) rbCOD removal (%) sbCOD removal (%) TN removal (%) TKN removal (%) Effluent N–NO_3^- (mg/L) Effluent N–NO_2^- (mg/L) TP removal (%) Effluent turbidity (NTU)	[136]
2011	CCD	Design-Expert v6.0	Synthetic wastewater	AS & RBC	HRT (h) COD/N (mg/L) Internal recirculation from aerobic to anoxic zone (R) Disks rotating speed (rpm)	COD removal (%) TKN removal (%) TN removal (%) Denitrification (%) NO_3 effluent (mg/L) P removal (%) Effluent turbidity (NTU)	[112]
2009	CCD	MINITAB v14 and MATLAB v7	Biological wastewater	Standard A^2O process	Internal recycling DO set point Wasted sludge	TN removal (%) TP removal (%)	[113]

Table 6
Application of RSM in lagoon processes

Year	RSM		Biological treatment process		Model		References
	Design method	Software	Wastewater type	Method	Parameters	Responses	
2019	CCD	Design-Expert v6.0.6	Petroleum industry wastewater	Facultative stabilization pond	HRT (day) Phenol concentration (mg/L)	SCOD removal (%) TCOD removal (%) Total biochemical oxygen demand ($TBOD_5$) removal (%) Soluble biochemical oxygen demand ($SBOD_5$) removal (%) Phenol removal (%)	[138]
2018	CCD	Design-Expert v10	Synthetic wastewater	Stabilization ponds	Temperature (°C) Phenol concentration (mg/L)	Phenol removal (%)	[137]
2017	CCD	Design-Expert v6.0.6	Oil refinery wastewater	Stabilization ponds	Phenol concentration (mg/L) Temperature (°C) HRT (day)	TCOD removal (%) SCOD removal (%) $TBOD_5$ removal (%) $SBOD_5$ removal (%) $N–NH_3$ removal (%) $P–PO_4$ removal (%) Phenol removal (%) N/P out	[139]
	BBD	Design-Expert v7.0	Real piggery wastewater	Stabilization ponds	pH Temperature (°C) Retention time (day)	COD removal (%)	[140]
2013	BBD	–	–	Constructed wetland	Temperature (°C) Filler thickness (cm) Filler size (mm)	Ammonia oxidation rate (AOR) (%) Nitrite accumulation rate (NAR) (%)	[141]

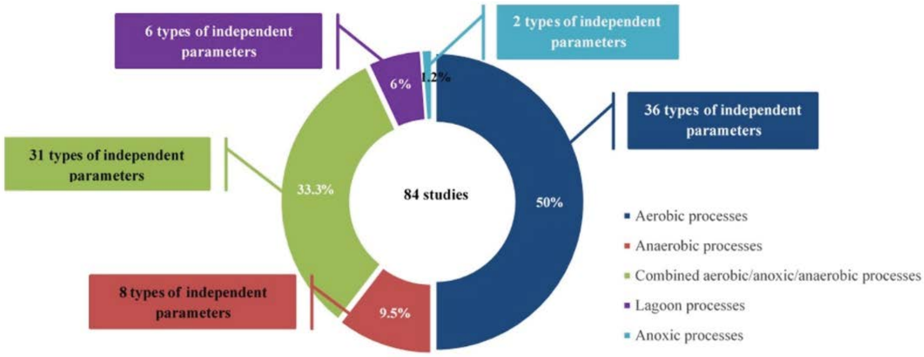


Fig. 5. Major biological processes percentage and types of independent parameters used for RSM design.

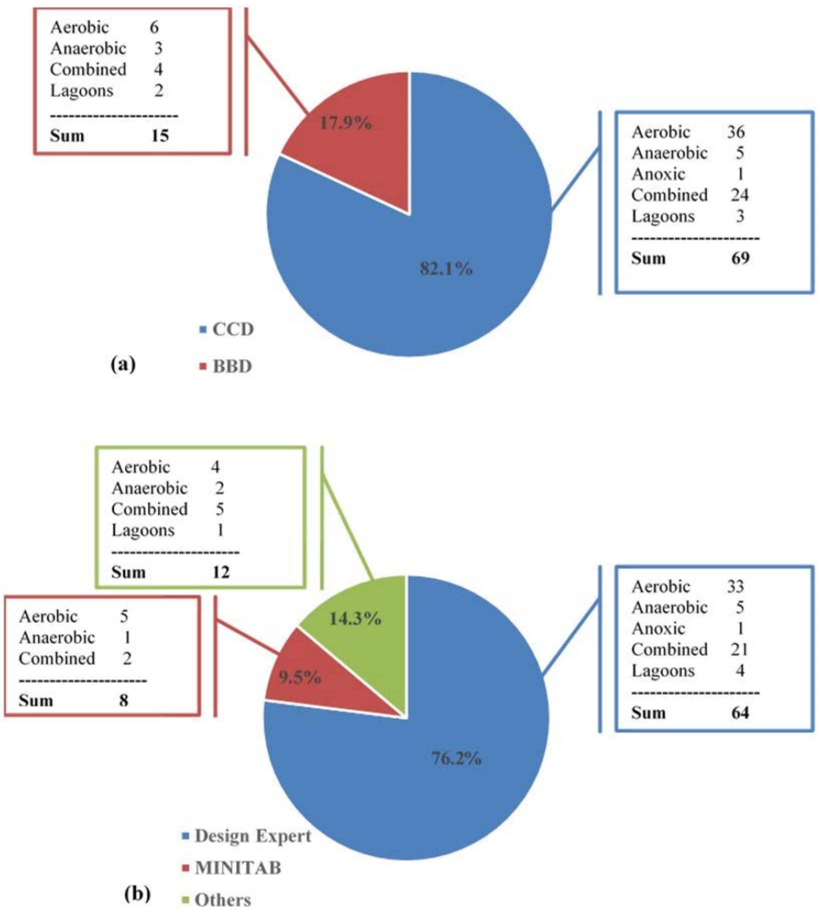


Fig. 6. Pie charts of RSM characteristics used in the chosen 84 papers according to each major biological treatment method: (a) number of RSM methods and (b) number of used software.

initial pH, respectively. Some other parameters such as DO (mg/L), aeration position, disks rotating speed, bead diameter, type of carrier, and so forth were used once in some special conditions which were classified as others in Table 7. All of the other parameters are presented in Table A1.

According to Tables 3–6, more than 58% of the articles used 3 parameters in the design of RSM through CCD and BBD. Also, about 27% and 11% of papers were used 2 and 4 parameters, respectively, and approximately 4% of papers applied 5 factors using the CCD method. According to Fig. 6, 82% of 84 papers employed the CCD approach that could be related to the capability of this approach. CCD approach could accurately fit a full-quadratic and linear model by evaluating five levels of variables, consider extreme variable combinations with an effective approximation of first and second-order polynomial terms. The BBD approach was used in about 18% of the papers, which could be attributed to the lack of extreme variable combinations in

Table 7
Number of the most prominnet evaluated parameters using RSM for each biological processes (84 studies)

Type of parameters in each major biological process	Type of biological treatment process							
	Aerobic			Anaerobic	Anoxic	Combined	Lagoons	Total number of parameters in 84 studies
Initial pollutant concentration (mg/L)	12 5 1	18	4 1 3	8	2	12	3	43
HRT (Retention time or contact time) (h or day)	11 8 2	21	2 1 1	4	1	14	3	43
Biomass (MLSS or MLVSS) concentration (mg/L)	11 3	14		–	–	6	–	20
Air flow rate/aeration rate [(mL/min) or (m^3/h) or (L/min) or (L/h)]	8 4 2	14		–	–	4	–	18
SRT (day)	2 1 1	4		–	–	2	–	6
Temperature (°C)	3 1 1 1	6	3 1	4	–	1	4	15
Initial pH	3 1	4	2 1	3	–	3	1	11
Others[a]	31 11 2 3	47	4	4	–	44	2	97
–	AS, MBR, MBBR, RBC or TF		UASB, Anaerobic contact processes, Anaerobic digestion, Anammox/UASB			–		

[a]Parameters that were not frequently applied or applied once among 84 studies according to the specific condition of a process are categorized as others.

comparison with CCD and no examination of borderline regions, leading to a lower number of degrees of freedom.

As presented in Fig. 6, 76% of the papers incorporated Design-Expert software to simulate and optimize the biological processes through RSM. The majority usage of Design-Expert was because of its specialty in DOE as well as its user-friendliness. MINITAB was also applied in about 10% of the papers. Other software such as MATLAB and the researches that did not mention the type of software was categorized in the "other" section. Detailed information of the RSM method and software applied in 84 studies are presented in Table A2.

4. Conclusion and future perspectives

The current study reviewed 84 papers of RSM application in major biological treatment processes, including aerobic, anaerobic, anoxic, combined, and lagoon processes. Amongst different DOE methods, the application of RSM for biological processes, initiated in 2009, was significantly grown in the last two decades; and the most published papers belonged to 2014 and 2017. According to the current review, regardless of RSM restrictions (like errors with discrete parameters and imprecision of extrapolation beyond experimental limits), numerous researchers have applied it as a convenient tool for designing, modeling, predicting, and optimizing the biological wastewater treatment processes with satisfactory precision. Consequently, most of the journals in the environmental engineering field have a fruitful history in publishing papers related to applying RSM in biological treatment methods. But there has been no thorough review paper to sum up the application of RSM in biological treatment processes to achieve its milestones in future studies.

According to the systematic approach, the most application of RSM in biological processes were in the aerobic, the combined, and the anoxic processes, respectively. In the last two decades, about 47 journals had contributed to publishing the 84 papers, and "Desalination and Water Treatment" and "Bioresource Technology" was in the top with 13 and 7 papers, respectively. Furthermore, Quartiles rank of more than 70% of the journals were Q1 and Q2. As a result, the application of RSM in biological wastewater treatment processes has been mainly applied by developing countries more than that of developed countries. The largest number of studies were conducted in Iran, with 36 publications; Furthermore, China, Malaysia, and India, altogether, also published more than 30 papers in this field. The Razi University of Iran was on the top list of universities/research centers that published more studies in this field.

According to the critical approach, more than 80% of the 84 papers applied the CCD approach of RSM, which is related to the capabilities of this approach. The majority of researchers evaluated three or less parameters; and the predominant parameters in all biological processes were initial pollutant concentration, HRT (h or day), biomass concentration, and airflow rate. In addition, most of the selected papers had more than one response, and the pollutant removal efficiency was the most popular response. As convenient software for the RSM, Design-Expert and MINITAB were mostly applied.

The appropriate RSM application could provide outstanding design and optimization of biological wastewater treatment processes. Also, based on the obtained results of this paper, the main gaps of this field will be mentioned as follows:

- Further research to understand the design capabilities of strategies other than CCD to researches with a high number of parameters due to the nature of biological wastewater treatment.
- More evaluation on utilizing the RSM to model the real biological wastewaters (Municipal/Industrial) to investigate this methodology's capability in real environments.
- Noticing other responses along with the pollutant removal efficiency, like cost, is highly encouraged. In this rule, techno-economical evaluation research could be useful for further studies in this field.
- Presenting several optimization scenarios via a "multi-response optimization approach" can be investigated as prospective researches. This approach can expand the logic of optimization in various possibilities, resulting in a well-understanding process.

These research gaps will be valuable to those who are generally involved in the application of biological treatment processes and RSM for their future research perspectives.

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References

[1] S. Rana, N. Gupta, R.S. Rana, Removal of Organic pollutant with the use of Rotating Biological Contactor, Mater. Today:. Proc., 5 (2018) 4218–4224.

[2] S. Zinadini, M. Rahimi, A.A. Zinatizadeh, Z.S. Mehrabadi, High frequency ultrasound-induced sequence batch reactor as a practical solution for high rate wastewater treatment, J. Environ. Chem. Eng., 3 (2015) 217–226.

[3] Metcalf & Eddy, Inc., Wastewater Engineering: Treatment and Reuse, 5th ed., McGraw-Hill Education, United States of America, 2014.

[4] M.R. Alavi Maghaddam, H. Satoh, T. Mino, Effect of important operational parameters on performance of coarse pore filtration activated sludge process, Water Sci. Technol., 46 (2002a) 229–236.

[5] M.R. Alavi Moghaddam, H. Satoh, T. Mino, Performance of coarse pore filtration activated sludge system, Water Sci. Technol., 46 (2002b) 71–76.

[6] M.R. Alavi Moghaddam, Y. Guan, H. Satoh, T. Mino, Performance and microbial dynamics in the coarse pore filtration activated sludge process at different SRTs (solids retention times), Water Sci. Technol., 47 (2003) 73–80.

[7] M.R. Alavi Moghaddam, Y. Guan, H. Satoh, T. Mino, Filter clogging in coarse pore filtration activated sludge process under high MLSS concentration, Water Sci. Technol., 54 (2006) 55–66.

[8] A.K. Orhon, K.B. Orhon, U. Yetis, F.B. Dilek, Fate of triclosan in laboratory-scale activated sludge reactors - effect of culture acclimation, J. Environ. Manage., 216 (2018) 320–327.

[9] A.A. Vaigan, M.R. Alavi Moghaddam, H. Hashemi, Aerobic sequencing batch reactor system with granular activated carbon for the treatment of wastewater containing a reactive dye, Environ. Eng. Manage. J., 9 (2010) 407–411.

[10] M. Bagheri, S.A. Mirbagheri, Critical review of fouling mitigation strategies in membrane bioreactors treating water and wastewater, Bioresour. Technol., 258 (2018) 318–334.

[11] N. Fallah, B. Bonakdarpour, B. Nasernejad, M.R. Alavi Moghadam, Long-term operation of submerged membrane bioreactor (MBR) for the treatment of synthetic wastewater containing styrene as volatile organic compound (VOC): effect of hydraulic retention time (HRT), J. Hazard. Mater., 178 (2010) 718–724.

[12] M. Hasani Zonoozi, M.R. Alavi Moghaddam, R. Maknoon, Investigation of HRT effects on membrane fouling in sequencing batch membrane bioreactor with respect to batch filtration mode, Environ. Prog. Sustainable Energy, 36 (2017) 1785–1793.

[13] M. Hasani Zonoozi, M.R. Alavi Moghaddam, R. Maknoon, Operation of integrated sequencing batch membrane bioreactor treating dye-containing wastewater at different SRTs: study of overall performance and fouling behavior, Environ. Sci. Pollut. Res., 22 (2015) 5931–5942.

[14] M. Hasani Zonoozi, M.R. Alavi Moghaddam, R. Maknoon, Decolorization kinetics and characteristics of the azo dye acid red 18 in MSBR system at various HRTs and SRTs, Membr. Water Treat., 5 (2014) 281–293.

[15] V. Jegatheesan, B.K. Pramanik, J.Y. Chen, D. Navaratna, C.-Y. Chang, L. Shu, Treatment of textile wastewater with membrane bioreactor: a critical review, Bioresour. Technol., 204 (2016) 202–212.

[16] S.N.H.A. Bakar, H.A. Hasan, A.W. Mohammad, S.R.S. Abdullah, T.Y. Haan, R. Ngteni, K.M.M. Yusof, A review of moving-bed biofilm reactor technology for palm oil mill effluent treatment, J. Cleaner Prod., 171 (2018) 1532–1545.

[17] E. Hosseini Koupaie, M.R. Alavi Moghaddam, H. Hashemi, Comparison of overall performance between moving-bed and conventional sequencing batch reactor, Iran. J. Environ. Health Sci. Eng., 8 (2011a) 235–244.

[18] A. Saha, S. Bhushan, P. Mukherjee, C. Chanda, M. Bhaumik, M. Ghosh, J. Sharmin, P. Datta, S. Banerjee, P. Barat, A.R. Thakur, L.M. Gantayet, I. Mukherjee, S.R. Chaudhuri, Simultaneous sequestration of nitrate and phosphate from wastewater using a tailor-made bacterial consortium in biofilm bioreactor, J. Chem. Technol. Biotechnol., 93 (2018) 1279–1289.

[19] P. Rybarczyk, B. Szulczyński, J. Gębicki, J. Hupka, Treatment of malodorous air in biotrickling filters: a review, Biochem. Eng. J., 141 (2018) 146–162.

[20] Q. Zhang, F.Y. Ji, X.Y. Xu, Optimization of nitrate removal from wastewater with a low C/N ratio using solid-phase denitrification, Environ. Sci. Pollut. Res. Int., 23 (2016) 698–708.

[21] T. Najib, M. Solgi, A. Farazmand, S.M. Heydarian, B. Nasernejad, Optimization of sulfate removal by sulfate reducing bacteria using response surface methodology and heavy metal removal in a sulfidogenic UASB reactor, J. Environ. Chem. Eng., 5 (2017) 3256–3265.

[22] R. Camarillo, J. Rincón, Effect of inhibitory compounds on the two-phase anaerobic digestion performance of diluted wastewaters from the alimentary industry, J. Chem. Technol. Biotechnol., 84 (2009) 1615–1623.

[23] G. Wang, X.C. Xu, Z. Gong, F. Gao, F.L. Yang, H.M. Zhang, Study of simultaneous partial nitrification, ANAMMOX and denitrification (SNAD) process in an intermittent aeration membrane bioreactor, Process Biochem., 51 (2016) 632–641.

[24] Y.Y. Ren, M. Yu, C.F. Wu, Q.H. Wang, M. Gao, Q.Q. Huang, Y. Liu, A comprehensive review on food waste anaerobic digestion: research updates and tendencies, Bioresour. Technol., 247 (2018) 1069–1076.

[25] A. Azizi, M.R. Alavi Moghaddam, R. Maknoon, E. Kowsari, Comparison of three combined sequencing batch reactor followed by enhanced Fenton process for an azo dye degradation: bio-decolorization kinetics study, J. Hazard. Mater., 299 (2015a) 343–350.

[26] A. Azizi, M.R. Alavi Moghaddam, R. Maknoon, E. Kowsari, Innovative combined technique for high concentration of azo dye AR18 wastewater treatment using modified SBR and enhanced Fenton process as post treatment, Process Saf. Environ. Prot., 95 (2015b) 255–264.

[27] A.A. Forbis-Stokes, L. Rocha-Melogno, M.A. Deshusses, Nitrifying trickling filters and denitrifying bioreactors for nitrogen management of high-strength anaerobic digestion effluent, Chemosphere, 204 (2018) 119–129.

[28] M. Hakimelahi, M.R. Alavi Moghaddam, S.H. Hashemi, Comparison of different duration of anaerobic and aerobic phases on acid red 18 removal in sequencing batch reactors, Environ. Eng. Manage. J., 15 (2016) 2529–2535.

[29] M. Hakimelahi, M.R. Alavi Moghaddam, S.H. Hashemi, Biological treatment of wastewater containing an azo dye using mixed culture in alternating anaerobic/aerobic sequencing batch reactors, Biotechnol. Bioprocess Eng., 17 (2012) 874–880.

[30] E. Hosseini Koupaie, M.R. Alavi Moghaddam, S.H. Hashemi, Evaluation of integrated anaerobic/aerobic fixed-bed sequencing batch biofilm reactor for decolorization and biodegradation of azo dye Acid Red 18: comparison of using two types of packing media, Bioresour. Technol., 127 (2013a) 415–421.

[31] E. Hosseini Koupaie, M.R. Alavi Moghaddam, S.H. Hashemi, Successful treatment of high azo dye concentration wastewater using combined anaerobic/aerobic granular activated carbon-sequencing batch biofilm reactor (GAC-SBBR): simultaneous adsorption and biodegradation processes, Water Sci. Technol., 67 (2013b) 1816–1821.

[32] E. Hosseini Koupaie, M.R. Alavi Moghaddam, S.H. Hashemi, Investigation of decolorization kinetics and biodegradation of azo dye Acid Red 18 using sequential process of anaerobic sequencing batch reactor/moving bed sequencing batch biofilm reactor, Int. Biodeterior. Biodegrad., 71 (2012) 43–49.

[33] E. Hosseini Koupaie, M.R. Alavi Moghaddam, S.H. Hashemi, Post-treatment of anaerobically degraded azo dye Acid Red 18 using aerobic moving bed biofilm process: enhanced removal of aromatic amines, J. Hazard. Mater., 195 (2011b) 147–154.

[34] Y. Liu, J.-H. Tay JH, State of the art of biogranulation technology for wastewater treatment, Biotechnol. Adv., 22 (2004) 533–563.

[35] S. Sadri Moghaddam, M.R. Alavi Moghaddam, Aerobic granular sludge for dye biodegradation in a sequencing batch reactor with anaerobic/aerobic cycles, CLEAN Soil Air Water, 44 (2016) 438–443.

[36] S. Sadri Moghaddam, M.R. Alavi Moghaddam, Cultivation of aerobic granules under different pre-anaerobic reaction times in sequencing batch reactors, Sep. Purif. Technol., 142 (2015) 149–154.

[37] S. Sadri Moghaddam, M.R. Alavi Moghaddam, Investigating the influence of elongated anaerobic feeding strategy on aerobic sludge granulation and characteristics in sequencing batch reactor, Water Sci. Technol., 70 (2014) 249–255.

[38] C.H. Shin, J.H. Bae, Current status of the pilot-scale anaerobic membrane bioreactor treatments of domestic wastewaters: a critical review, Bioresour. Technol., 247 (2018) 1038–1046.

[39] S. Mehrali, M.R. Alavi Moghaddam, S.H. Hashemi, Feasibility study of several cyclic anaerobic/aerobic conditions in SBR system for treating of simulated dye (reactive blue19) wastewater, Environ. Eng. Manage. J., 11 (2012) 617–621.

[40] A.T. Nair, A.R. Makwana, M.M. Ahammed, The use of response surface methodology for modelling and analysis of water and wastewater treatment processes: a review, Water Sci. Technol., 69 (2014) 464–478.

[41] D.C. Montgomery, Design and Analysis of Experiments, 9th ed., John Wiley & Sons, Hoboken, New Jersey, United States, 2017.

[42] E. Nazlabadi, M.R. Alavi Moghaddam, E. Karamati-Niaragh, Simultaneous removal of nitrate and nitrite using electrocoagulation/floatation (ECF): a new multi-response optimization approach, J. Environ. Manage., 250 (2019) 109489, doi: 10.1016/j.jenvman.2019.109489.

[43] Engineering Statistics e-Handbook, NIST/SEMATECH e-Handbook of Statistical Methods. Available at: http://www.itl.nist.gov/div898/handbook/, Access Date: 2019.

[44] S. Karimifard, M.R. Alavi Moghaddam, Application of response surface methodology in physicochemical removal of dyes from wastewater: a critical review, Sci. Total Environ., 640 (2018) 772–797.

[45] A.I. Khuri, J.A. Cornell, Response Surfaces: Designs and Analyses, Marcel Dekker, New York, 1987.

[46] R.H. Myers, D.C. Montgomery, C.M. Anderson-Cook, Response Surface Methodology: Process and Product Optimization Using Designed Experiments, John Wiley & Sons, Hoboken, New Jersey, United States, 2016.
[47] G.E.P. Box, K.B. Wilson, On the experimental attainment of optimum conditions, J. R. Stat. Soc. Ser. B Stat. Methodol., 13 (1951) 1–38.
[48] R. Mead, D.J. Pike, A biometrics invited paper. A review of response surface methodology from a biometric viewpoint, Biometrics, 31 (1975) 803–851.
[49] G.E.P. Box, Design and Analysis of Industrial Experiments, O.L. Davies, Ed., Oliver and Boyd (for Imperial Chemical Industries Ltd.), London and Edinburgh, 1954, pp. xiii + 636.
[50] W.J. Hill, W.G. Hunter, A review of response surface methodology: a literature survey, Technometrics, 8 (1966) 571–590.
[51] G.E.P. Box, The exploration and exploitation of response surfaces: some general considerations and examples, Biometrics, 10 (1954) 16–60.
[52] R.A. Bradley, Determination of optimum operating conditions by experimental methods, Part I, Ind. Qual. Control, 15 (1958) 16.
[53] J.S. Hunter, Determination of optimum conditions by experimental methods, Part II–1, Ind. Qual. Control, 15 (1958) 16.
[54] J.S. Hunter, Determination of optimum conditions by experimental methods, Part II–2, Ind. Qual. Control, 15 (1959a) 7.
[55] J.S. Hunter, Determination of optimum conditions by experimental methods, Part II–3, Ind. Qual. Control, 15 (1959b) 6.
[56] W.G. Cochran, G.M. Cox, Experimental Designs, John Wiley & Sons, New York, 1957, p. 335.
[57] G.H. Box, W.G. Hunter, J.S. Hunter, Statistics for Experimenters, John Wiley & Sons, New York, 1978.
[58] W.J. Diamond, Practical Experimental Designs for Engineers and Scientists, 2nd ed., Wiley, New York, 1989.
[59] M.B. Salehi, M.V. Sefti, A.M. Moghadam, A.D. Koohi, Study of salinity and pH effects on gelation time of a polymer gel using central composite design method, J. Macromol. Sci. Part B Phys., 51 (2012) 438–451.
[60] P.W.M. John, Statistical Design and Analysis of Experiments, Society for Industrial and Applied Mathematics, University City Science Center, Philadelphia, 1998.
[61] G.E. Box, N.R. Draper, Empirical Model-Building and Response Surfaces, John Wiley & Sons, England, 1987.
[62] Scopus, Scopus Content Coverage Guide, Elsevier, Netherlands, August 2017.
[63] N. Karami, P. Mohammadi, A. Zinatizadeh, F. Falahi, N. Aghamohammadi, High rate treatment of hospital wastewater using activated sludge process induced by high-frequency ultrasound, Ultrason. Sonochem., 46 (2018) 89–98.
[64] M. Pirsaheb, M. Mohamadi, A.M. Mansouri, A.A.L. Zinatizadeh, S. Sumathi, K. Sharafi, Process modeling and optimization of biological removal of carbon, nitrogen and phosphorus from hospital wastewater in a continuous feeding & intermittent discharge (CFID) bioreactor, Korean J. Chem. Eng., 32 (2015) 1340–1353.
[65] N. Abedinzadeh, M. Shariat, S.M. Monavari, A. Pendashteh, Evaluation of color and COD removal by Fenton from biologically (SBR) pre-treated pulp and paper wastewater, Process Saf. Environ. Prot., 116 (2018) 82–91.
[66] A. Barwal, R. Chaudhary, Application of response surface methodology to optimize the operational parameters for enhanced removal efficiency of organic matter and nitrogen: moving bed biofilm reactor, Environ. Sci. Pollut. Res., 23 (2016) 9944–9955.
[67] H. Farraji, N.Q. Zaman, H.A. Aziz, S.K.M. Sa'at, Palm oil mill effluent and municipal wastewater co-treatment by zeolite augmented sequencing batch reactors: turbidity removal, AIP Conf. Proc., 1892 (2017) 040013, doi: 10.1063/1.5005693.
[68] H.-Y. Fu, P.-C. Xu, G.-H. Huang, T. Chai, M. Hou, P.-F. Gao, Effects of aeration parameters on effluent quality and membrane fouling in a submerged membrane bioreactor using Box–Behnken response surface methodology, Desalination, 302 (2012) 33–42.
[69] S. Ibrahim, N.A. Wahab, A.N. Anuar, M. Bob, Parameter optimisation of aerobic granular sludge at high temperature using response surface methodology, Int. J. Electr. Comput. Eng., 7 (2017) 1522–1529.
[70] M. Jamshidi, A.A. Zinatizadeh, S. Rezaee, A. Asadi, Process performance of a granular single bioreactor with continuous feeding and intermittent discharge regime treating dairy wastewater, Int. J. Eng., 32 (2019) 10–17.
[71] A. Asadi, A.A.L. Zinatizadeh, S. Sumathi, N. Rezaie, S. Kiani, A comparative study on performance of two aerobic sequencing batch reactors with flocculated and granulated sludge treating an industrial estate wastewater: process analysis and modeling, Int. J. Eng. Trans. B Appl., 26 (2012) 105–116.
[72] F.K. Banaei, A.A.L. Zinatizadeh, M. Mesgar, Z. Salari, S. Sumathi, Effect of biomass concentration and aeration rate on performance of a full-scale industrial estate wastewater treatment plant, J. Environ. Chem. Eng., 1 (2013) 1144–1153.
[73] A. Mojiri, H.A. Aziz, N.Q. Zaman, S.Q. Aziz, M.A. Zahed, Metals removal from municipal landfill leachate and wastewater using adsorbents combined with biological method, Desal. Water Treat., 57 (2016) 2819–2833.
[74] D.-X. Hu, Y. Tian, Z.-B. Chen, H. Ge, Y.-B. Cui, C.-Q. Ran, Improving the simultaneous removal of chemical oxygen demand and terephthalic acid in a cross-flow aerobic sludge reactor by using response surface methodology, Water Sci. Technol., 71 (2015) 1823–1830.
[75] M. Rajasimman, S.V. Babu, N. Rajamohan, Biodegradation of textile dyeing industry wastewater using modified anaerobic sequential batch reactor – start-up, parameter optimization and performance analysis, J. Taiwan Inst. Chem. Eng., 72 (2017) 171–181.
[76] S. Sathian, M. Rajasimman, G. Radha, V. Shanmugapriya, C. Karthikeyan, Performance of SBR for the treatment of textile dye wastewater: optimization and kinetic studies, Alexandria Eng. J., 53 (2014) 417–426.
[77] C.F. Bustillo-Lecompte, M. Mehrvar, Treatment of an actual slaughterhouse wastewater by integration of biological and advanced oxidation processes: modeling, optimization, and cost-effectiveness analysis, J. Environ. Manage., 182 (2016) 651–666.
[78] S.C. Azimi, F. Shirini, A. Pendashteh, Evaluation of COD and turbidity removal from woodchips wastewater using biologically sequenced batch reactor, Process Saf. Environ. Prot., 128 (2019) 211–227.
[79] V.G. Khondabi, A. Fazlali, M. Arjomandzadegan, Biological treatment of phenol from petroleum refinery wastewater using mixed indigenous cultures in a rotating biological contactor: experimental and statistical studies, Desal. Water Treat., 160 (2019) 135–143.
[80] M. Ahmadi, N. Amiri, M. Pirsaheb, P. Amiri, Application of the central composite design for the treatment of soft drink factory wastewater in two-stage aerobic sequencing batch reactors combined with ozonation, Desal. Water Treat., 57 (2016) 19077–19086.
[81] M. Amini, H. Younesi, G. Najafpour, A.A. Zinatizadeh-Lorestani, Application of response surface methodology for simultaneous carbon and nitrogen (SND) removal from dairy wastewater in batch systems, Int. J. Environ. Stud., 69 (2012) 962–986.
[82] E. Ashrafi, A.M. Zeinabad, S.M. Borghei, E. Torresi, J.M. Sierra, Optimising nutrient removal of a hybrid five-stage Bardenpho and moving bed biofilm reactor process using response surface methodology, J. Environ. Chem. Eng., 7 (2019) 102861, doi: 10.1016/j.jece.2018.102861.
[83] A. Barwal, R. Chaudhary, Optimization of operational parameters in moving bed biofilm reactor with low cost polystyrene biocarrier by the response surface method, Water Qual. Res. J. Can., 52 (2017) 26–41.
[84] M.D. Chang, Y.Z. Wang, Y. Pan, K. Zhang, L.T. Lyu, M. Wang, T. Zhu, Nitrogen removal from wastewater via simultaneous nitrification and denitrification using a biological folded non-aerated filter, Bioresour. Technol., 289 (2019) 121696, doi: 10.1016/j.biortech.2019.121696.
[85] L. Chen, C.Q. Cao, Characteristics and simulation of soluble microbial products in membrane bioreactors coupled with moving carriers (MBR-MC), Desal. Water Treat., 40 (2012) 45–55.

[86] R. Darvishi Cheshmeh Soltani, A. Rezaee, A.R. Khataee, H. Godini, Optimisation of the operational parameters during a biological nitrification process using response surface methodology, Can. J. Chem. Eng., 92 (2014) 13–22.
[87] S. Dey, S. Mukherjee, Performance study and kinetic modeling of hybrid bioreactor for treatment of bi-substrate mixture of phenol-m-cresol in wastewater: process optimization with response surface methodology, J. Environ. Sci.-China, 25 (2013) 698–709.
[88] M. Mirghorayshi, A.A. Zinatizadeh, M. Van Loosdrecht, Evaluating the process performance and potential of a high-rate single airlift bioreactor for simultaneous carbon and nitrogen removal through coupling different pathways from a nitrogen-rich wastewater, Bioresour. Technol., 260 (2018) 44–52.
[89] T.P. Nguyen, N. Hilal, N.P. Hankins, Operating conditions corresponding to optimal final properties of activated sludge using the DOE and RSM techniques, Sep. Sci. Technol., 44 (2009) 2041–2066.
[90] F. Qaderi, A.H. Sayahzadeh, M. Azizi, Efficiency optimization of petroleum wastewater treatment by using of serial moving bed biofilm reactors, J. Cleaner Prod., 192 (2018) 665–677.
[91] Z.S. Mehrabadi, A.A.L. Zinatizadeh, Performance of a compartmentalized activated sludge (CAS) system treating a synthetic antibiotics industrial wastewater (SAW), J. Water Process Eng., 3 (2014) 26–33.
[92] S.N. Shim, S.-R. Kim, S.J. Jo, K.-M. Yeon, C.-H. Lee, Evaluation of mechanical membrane cleaning with moving beads in MBR using Box–Behnken response surface methodology, Desal. Water Treat., 56 (2014) 2797–2806.
[93] R.K. Sonwani, G. Swain, B.S. Giri, R.S. Singh, B.N. Rai, A novel comparative study of modified carriers in moving bed biofilm reactor for the treatment of wastewater: process optimization and kinetic study, Bioresour. Technol., 281 (2019) 335–342.
[94] Y.Z. Wang, M.D. Chang, Y. Pan, K. Zhang, L.T. Lyu, M. Wang, T. Zhu, Performance analysis and optimization of ammonium removal in a new biological folded non-aerated filter reactor, Sci. Total Environ., 688 (2019) 505–512.
[95] V. Zeynali, J. Sargolzaei, A. Hedayati Moghaddam, S.M. Ali Masoudi, Implication of statistical design approach methodology for optimization of COD removal, effluent quality, and biosludge settling properties in aerobic bioreactors, Environ. Prog. Sustainable Energy, 36 (2017) 1428–1438.
[96] V. Zeynali, J. Sargolzaei, A. Hedayati Moghaddam, Optimization of several hydrodynamic and non-hydro-dynamic operating parameters in treatment of synthetic wastewater containing wheat starch in a sequencing batch reactor (SBR) using response surface methodology, Desal. Water Treat., 57 (2016) 24240–24256.
[97] L. Zhou, B. Peng, K. Xiao, Role of micronutrients on dyeing wastewater treatment in activated sludge process, Water Environ. Res., 89 (2017) 221–227.
[98] A.A.L. Zinatizadeh, Y. Mansouri, A. Akhbari, S. Pashaei, Biological treatment of a synthetic dairy wastewater in a sequencing batch biofilm reactor: statistical modeling using optimization using response surface methodology, Chem. Ind. Chem. Eng. Q., 17 (2011) 485–495.
[99] S. Saha, N. Badhe, S. Pal, R. Biswas, T. Nandy, Carbon and nutrient-limiting conditions stimulate biodegradation of low concentration of phenol, Biochem. Eng. J., 126 (2017) 40–49.
[100] A. Mojiri, H.A. Aziz, N.Q. Zaman, S.Q. Aziz, M.A. Zahed, Powdered ZELIAC augmented sequencing batch reactors (SBR) process for co-treatment of landfill leachate and domestic wastewater, J. Environ. Manage., 139 (2014) 1–14.
[101] A.A. Zinatizadeh Lorestani, H. Bashiri, A. Asadi, H. Bonakdari, Comparison of different fluid dynamics in activated sludge system for the treatment of a stimulated milk processing wastewater: process analysis and optimization, Korean J. Chem. Eng., 29 (2012) 1352–1361.
[102] A.A. Zinatizadeh, H. Bonakdari, M. Pirsaheb, E. Gharacheh, Response surface analysis and statistical modeling of sulfide generation from municipal wastewater, CLEAN–Soil Air Water, 39 (2011) 444–459.
[103] R. Sridhar, V. Sivakumar, K. Thirugnanasambandham, Response surface modeling and optimization of upflow anaerobic sludge blanket reactor process parameters for the treatment of bagasse-based pulp and paper industry wastewater, Desal. Water Treat., 57 (2016) 4345–4356.
[104] P. Boonsawang, A. Rerngnarong, C. Tongurai, S. Chaiprapat, Effect of pH, OLR, and HRT on performance of acidogenic and methanogenic reactors for treatment of biodiesel wastewater, Desal. Water Treat., 54 (2015) 3317–3327.
[105] W. Kim, K.Y. Hwang, S.G. Shin, S.Y. Lee, S.W. Hwang, Effect of high temperature on bacterial community dynamics in anaerobic acidogenesis using mesophilic sludge inoculum, Bioresour. Technol., 101 (2010) S17–S22.
[106] X.-Y. Shi, D.-W. Jin, Q.-Y. Sun, W.-W. Li, Optimization of conditions for hydrogen production from brewery wastewater by anaerobic sludge using desirability function approach, Renewable Energy, 35 (2010) 1493–1498.
[107] A. Ndobeni, O. Oyekola, P.J. Welz, Organic removal rates and biogas production of an upflow anaerobic sludge blanket reactor treating sugarcane molasses, S. Afr. J. Chem. Eng., 28 (2019) 1–7.
[108] H. Chen, J.-J. Yu, X.-Y. Jia, R.-C. Jin, Enhancement of anammox performance by Cu(II), Ni(II) and Fe(III) supplementation, Chemosphere, 117 (2014) 610–616.
[109] B.-S. Xing, Q. Guo, Z.-Z. Zhang, J. Zhang, H.-Z. Wang, R.-C. Jin, Optimization of process performance in a granule-based anaerobic ammonium oxidation (anammox) upflow anaerobic sludge blanket (UASB) reactor, Bioresour. Technol., 170 (2014) 404–412.
[110] A. Srisuwun, N. Tantiwa, A. Kuntiya, A. Kawee-ai, A. Manassa, C. Techapun, P. Seesuriyachan, Decolorization of Reactive Red 159 by a consortium of photosynthetic bacteria using an anaerobic sequencing batch reactor (AnSBR), Prep. Biochem. Biotechnol., 48 (2018) 303–311.
[111] A.M. Mansouri, A.A. Zinatizadeh, A comparative study of an up-flow aerobic/anoxic sludge fixed film bioreactor and sequencing batch reactor with intermittent aeration in simultaneous nutrients (N, P) removal from synthetic wastewater, Water Sci. Technol., 76 (2017) 1044–1058.
[112] A. Akhbari, A.A.L. Zinatizadeh, P. Mohammadi, M. Irandoust, Y. Mansouri, Process modeling and analysis of biological nutrients removal in an integrated RBC-AS system using response surface methodology, Chem. Eng. J., 168 (2011) 269–279.
[113] M.H. Kim, A.S. Rao, C.K. Yoo, Dual optimization strategy for N and P removal in a biological wastewater treatment plant, Ind. Eng. Chem. Res., 48 (2009) 6363–6371.
[114] X. Zhou, Q. Zhang, H.L. Sun, Q.L. Zhao, Efficient nitrogen removal from synthetic domestic wastewater in a novel step-feed three-stage integrated anoxic/oxic biological aerated filter process through optimizing influent flow distribution ratio, J. Environ. Manage., 231(2019) 1277–1282.
[115] D.H. Choi, K.J. Cho, J.Y. Jung, Optimization of nitrogen removal performance in a single-stage SBR based on partial nitritation and ANAMMOX, Water Res., 162 (2019) 105–114.
[116] Y. Mortezaei, T. Amani, Sh. Elyasi, High-rate anaerobic digestion of yogurt wastewater in a hybrid EGSB and fixed-bed reactor: optimizing through response surface methodology, Process Saf. Environ. Prot., 113 (2018) 255–263.
[117] J. Jaafari, M. Seyedsalehi, G.H. Safari, M.E. Arjestan, H. Barzanouni, S. Ghadimi, H. Kamani, P. Haratipour, Simultaneous biological organic matter and nutrient removal in an anaerobic/anoxic/oxic (A^2O) moving bed biofilm reactor (MBBR) integrated system, Int. J. Environ. Sci. Technol., 14 (2017) 291–304.
[118] R. Shokoohi, A.J. Jafari, A. Dargahi, Z. Torkshavand, Study of the efficiency of bio-filter and activated sludge (BF/AS) combined process in phenol removal from aqueous solution: determination of removing model according to response surface methodology (RSM), Desal. Water Treat., 77 (2017) 256–263.
[119] C.F. Bustillo-Lecompte, M. Mehrvar, Treatment of actual slaughterhouse wastewater by combined anaerobic–aerobic processes for biogas generation and removal of organics and

nutrients: an optimization study towards a cleaner production in the meat processing industry, J. Cleaner Prod., 141 (2017) 278–289.
[120] A. Almasi, S.A. Mousavi, Z. Bahman, M.R. Zolfaghari, A.A. Zinatizadeh, Effect of hydraulic retention time and aeration time on the performance and microbial diversity in an upflow aerobic/anoxic sequential bioreactor, Desal. Water Treat., 57 (2016) 23589–23596.
[121] S. Rezaee, A.A.L. Zinatizadeh, A. Asadi, Comparative study on effect of mechanical mixing and ultrasound on the performance of a single up-flow anaerobic/aerobic/anoxic bioreactor removing CNP from milk processing wastewater, J. Taiwan Inst. Chem. Eng., 58 (2016) 297–309.
[122] S. Rezaee, A.A.L. Zinatizadeh, A. Asadi, High rate CNP removal from a milk processing wastewater in a single ultrasound augmented up-flow anaerobic/aerobic/anoxic bioreactor, Ultrason. Sonochem., 23 (2015) 289–301.
[123] X. Wu, J. Zhu, J.H. Cheng, N.W. Zhu, Optimization of three operating parameters for a two-step fed sequencing batch reactor (SBR) system to remove nutrients from swine wastewater, Appl. Biochem. Biotechnol., 174 (2015) 2857–2871.
[124] W. Dastyar, T. Amani, S. Elyasi, Investigation of affecting parameters on treating high-strength compost leachate in a hybrid EGSB and fixed-bed reactor followed by electrocoagulation–flotation process, Process Saf. Environ. Prot., 95 (2015) 1–11.
[125] A. Noroozi, M. Safari, N. Askari, Innovative hybrid-upflow sludge blanket filtration (H-USBF) combined bioreactor for municipal wastewater treatment using response surface methodology, Desal. Water Treat., 56 (2015) 2344–2350.
[126] F.-F. Qi, M.-H. Huang, Y. Zheng, Q. Xu, Optimization of an A^2/O process for tetracycline removal via response surface methodology coupled with a Box–Behnken design, J. Environ. Sci. Health. Part A Toxic/Hazard. Subst. Environ. Eng., 50 (2015) 735–743.
[127] S. Srinu Naik, Y. Pydi Setty, Optimization of parameters using response surface methodology and genetic algorithm for biological denitrification of wastewater, Int. J. Environ. Sci. Technol., 11 (2014) 823–830.
[128] Y.M. Li, J.T. Zou, L.L. Zhang, J. Sun, Aerobic granular sludge for simultaneous accumulation of mineral phosphorus and removal of nitrogen via nitrite in wastewater, Bioresour. Technol., 154 (2014) 178–184.
[129] H. Harun, A. Nor Anuar, Development and utilization of aerobic granules for soy sauce wastewater treatment: optimization by response surface methodology, J. Teknol., 69 (2014) 31–37.
[130] A.M. Mansouri, A.A. Zinatizadeh, M. Irandoust, A. Akhbari, Statistical analysis and optimization of simultaneous biological nutrients removal process in an intermittently aerated SBR, Korean J. Chem. Eng., 31 (2014) 88–97.
[131] A.N.D. Lima, B.M. Gomes, S.D. Gomes, K.Q.D. Carvalho, D. Christ, Application of response surface methodology to study the biological removal of nitrogen from effluent of cattle slaughterhouse in a sequencing batch reactor, Eng. Agr.-Jaboticabal., 34 (2014) 363–371.
[132] J.B.R. Mees, S.D. Gomes, S.C. Sampaio, S.D.M. Hasan, G.M.B. Caldereiro, C.S. de Cordovil, D.S. CM, Application of the response surface methodology for optimisation of biological nutrient removal from slaughterhouse effluents, J. Food Agric. Environ., 12 (2014) 786–792.
[133] A. Aris, K. Muda, M.R. Salim, Z. Ibrahim, COD and color removal from textile effluent using granular sludge biomass: effect of substrate and riboflavin, Desal. Water Treat., 52 (2014) 7366–7376.
[134] Y.J. Chan, C. Mei-Fong, L. Chung-Lim, Optimization of palm oil mill effluent treatment in an integrated anaerobic-aerobic bioreactor, Sustainable Environ. Res., 23 (2013) 153–170.
[135] M.H. Muhamad, S.R.S. Abdullah, A.B. Mohamad, R.A. Rahman, A.A.H. Kadhum, Application of response surface methodology (RSM) for optimisation of COD, NH_3–N and 2,4-DCP removal from recycled paper wastewater in a pilot-scale granular activated carbon sequencing batch biofilm reactor (GAC-SBBR), J. Environ. Manage., 121 (2013) 179–190.
[136] A. Asadi, A.A.L. Zinatizadeh, M.H. Isa, Performance of intermittently aerated up-flow sludge bed reactor and sequencing batch reactor treating industrial estate wastewater: a comparative study, Bioresour. Technol., 123 (2012) 495–506.
[137] F. Qaderi, A.H. Sayahzadeh, F. Azizpour, P. Vosughi, Efficiency modeling of serial stabilization ponds in treatment of phenolic wastewater by response surface methodology, Int. J. Environ. Sci. Technol., 16 (2019) 4193–4202.
[138] A. Almasi, M. Mahmoudi, M. Mohammadi, A. Dargahi, H. Biglari, Optimizing biological treatment of petroleum industry wastewater in a facultative stabilization pond for simultaneous removal of carbon and phenol, Toxin Rev., (2019) 1–9, doi: 10.1080/15569543.2019.1573433.
[139] A. Dargahi, M. Mohammadi, F. Amirian, A. Karami, A. Almasi, Phenol removal from oil refinery wastewater using anaerobic stabilization pond modeling and process optimization using response surface methodology (RSM), Desal. Water Treat., 87 (2017)199–208.
[140] B.U. Okoro, N.E. Nwaiwu, Optimization of waste stabilization pond performance for piggery waste treatment using response surface methodology, Environ. Res. Eng. Manage., 73 (2017) 52–61.
[141] G. Qin, Y. Li, Y. Han, J. Zhang, J. Zhou, L. Chen, B. Gong, Application of constructed wetland to partial nitrification process: relations betweenparameter values and effluent outcome using response surface methodology, J. Chem. Pharm., 5 (2013) 413–417.

Appendices

Table A1
Other parameters used in RSM of 84 studies

Biological process	Parameters used in RSM	
Aerobic	Flow rate (mL/min) or (L/h)	Mixing (min)
	Different wastewaters ratio (%)	Bead number
	Zn concentration (mg/L)	Bead diameter (mm)
	CO concentration (mg/L)	Disks rotating speed (rpm)
	Mo concentration (mg/L)	Flow rate (mL/min) or (L/h)
	Sorbent dosage (g/L)	Different wastewaters ratio (%)
	Ozone concentration was controlled as feed-gas and off-gas	Zn concentration (mg/L)
	Inlet H_2O_2 (mg/L)	CO concentration (mg/L)
	Calcium ion (mM)	Mo concentration (mg/L)
	Media filling ratio (%)	Sorbent dosage (g/L)
	Agitation rate (rpm)/rotational velocity (rpm)	Ozone concentration was controlled as feed-gas and off-gas
	COD/N/P ratio	Inlet H_2O_2 (mg/L)
	Impeller diameter	Calcium ion (mM)
	Organic loading rate (COD) (mg/L d)	Media filling ratio (%)
	Carbon source	Agitation rate (rpm)/rotational velocity (rpm)
	Biomass support (%, v/v)	COD/N/P ratio
	SLR (kg COD/(kg MLSS d))	Impeller diameter
	Internal recirculation from aerobic to anoxic zone (R)	Organic loading rate (COD) (mg/L d)
	Number of working aerators	Carbon source
	DO (mg/L)	Biomass support (%, v/v)
	$NH_4^+/NH_4^+NO_3$ ratio	SLR (kg COD/(kg MLSS d))
	Aeration position (cm)	Aeration time (h or min)
		Cycle time (h)/Cycling ratio/Exchange ratio
Anaerobic	Upflow velocity (m/h)	
	COD/SO_4^{2-} ratio	
	$COD_{ethanol}/COD_{total}$ ratio	
	Organic loading rate (OLR) (g COD/(L d))	
	Upflow velocity (m/h)	
Combined	COD/nitrogen ratio (COD/N)	Circulation rate (L/h)
	COD:N:P ratio	Operation time (day)
	DO (mg/L)	Organic loading rates (OLR) (g COD/L d)
	Glucose concentration (mg/L)	Internal recycling
	Nitrate recycle ratio	DO set point
	Aeration time mode	Wasted sludge
	F/M ratio	Influent C/N ratio
	First/second volumetric feeding ratio/First anaerobic/aerobic (an/oxic) time ratio/Second an/oxic time ratio	Flow rate (mL/min)
	Aeration mode	Ca concentration (mg/L)
	Substrate concentration (mg/L)	Anaerobic period (min)
	Biofilm carrier (g/L)	Aeration time (h or min)
	Carbon source (mg/L)	Cycle time (h)/Cycling ratio/Exchange ratio
Anoxic	–	
Lagoons	Filler thickness (cm)	
	Filler size (mm)	

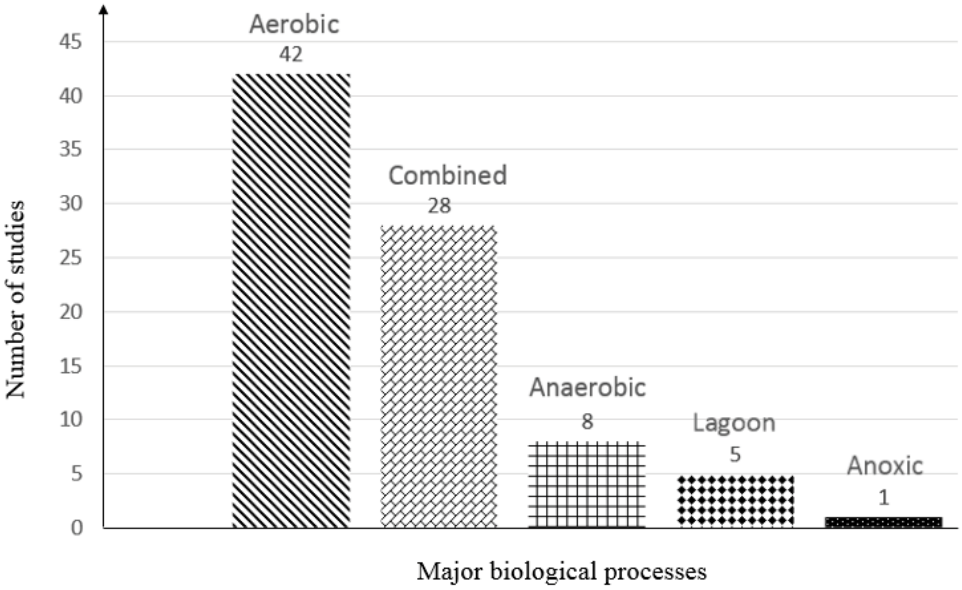

Fig. A1. Number of major biological processes in 84 selected papers according to [3].

Table A2
RSM method and software applied in 84 studies

Type of biological process	Number of RSM method		Number of software		
	CCD/CCF/CCR (CCC)	BBD	Design-Expert	MINITAB	Others
Aerobic	36	6	33	5	4
Anaerobic	5	3	5	1	2
Anoxic	1	–	1	–	–
Combined	24	4	21	2	5
Lagoons	3	2	4	–	1
Total %	82.1	17.9	76.2	9.5	14.3