Environmental Engineering and Management Journal

March 2015, Vol.14, No. 3, 533-539
http://omicron.ch.tuiasi.ro/EEMJ/

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SEPARATION OF SUCCINIC ACID FROM FERMENTATION BROTHS. MODELLING AND OPTIMIZATION

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Abstract

Succinic acid is widely used in different industries, its demand increasing each year. Therefore, efficiently producing it (especially from bio-regenerable sources) is an aspect that researchers try to solve thorough different methods, one of the approaches consisting in using process models for generating predictions and improving production by process optimization. In this work, a combination of two bio-inspired algorithms represented by Artificial Neural Networks and Clonal Selection was employed for determining optimal models for the separation of succinic acid from fermentation broths. Since these two algorithms cannot be naturally combined, a direct, real-value encoding for the most important model parameters was employed. In order to improve the performance of the general algorithm, a local hybrid search method based on Random Search and Back-Propagation was introduced into the optimization procedure. The results obtained showed that the algorithm improvements are translated into performance improvements.

Key words: back-propagation, clonal selection, neural network, random search, succinic acid

Received: November, 2014; Revised final: March, 2015; Accepted: March, 2015

1. Introduction

Models are adequate tools for system exploration, predictions, guidance, and optimization and, therefore, their use in solving real-life problems can help saving money and time (through reduction of materials required and experimental setups) (WU et al., 2008). Since a majority of the systems encountered in chemical engineering are non-convex, non-linear, and with constrained parameters, the classical approaches based on the chemical and physical laws often do not provide the required level of accuracy in the modelling attempt.

In this context, due to their interesting characteristics - capability of modelling non-linear relation, parallel processing, learning and fault tolerance -, neural networks (NNs) represent one of most used methods for replacing the phenomenological models, various studies on different chemical engineering aspects being performed (Curteanu and Cartwright, 2012; Curteanu et al., 2014; Dragoi et al., 2014; Gholikandi et al., 2014; Himmelblau, 2000; Suditu et al., 2013; Woinaroschy and Radu, 2014). Different types of networks were applied, the majority of works employing feed forward multiplayer perceptron (MLP) because it has a simple structure (simple interconnected neurons organized in layers) and can be applied to approximate virtually any smooth, measurable function. Consequently, the MLP neural network was used in this work for modelling an important bio-chemical process.

Although simple and easy to use, the NNs have a critical shortcoming related to the lack of robustness when improper architecture, training and validation procedures are used (Noor et al., 2010). In

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order to solve this problem and to overcome the gradient descent based training shortcomings, neuro-evolution (evolving neural networks with evolutionary algorithms) can be applied. In this work, the idea of neuro-evolution is taken further, the alteration and optimization of neural networks being performed with an Artificial Immune System (AIS) algorithm represented by Clonal Selection (CS).

The AIS algorithms can be applied to various types of problems, the domains where is most used, ordered descending based on the number of applications are: clustering/classification, anomaly detection, computer security, numeric function optimization, combinatory optimization, learning, bio-informatics, image processing, robotics, control, virus detection, web mining (Hart and Timmis, 2005). Other applications are represented by: pattern recognition, scheduling control, machine learning, reasoning, emergent behavior (Khilwani et al., 2008; Tan et al., 2008).

Regarding the applications of AIS in the chemical engineering field, there are only a few works, in the latest years, a rising use trend being observed. For example, Hu and Yan (2009) used the principles of the artificial immune system to auto-adapt the parameters of the differential evolution algorithm, the combination being applied for the kinetic parameters estimation of the homogenous mercury oxidation. Similarly, a hybridization of a fuzzy –based adaptive genetic algorithm with a new variant of AIS - fuzzy theory, is applied for parameter estimation of a reaction dynamic model of the low temperature SO_2 oxidation, using Cs-Rb-V sulfuric acid catalyst (Yang and Yan, 2011). Another combination of algorithms (AIS and dynamic time warping) was used for the diagnosis of batch chemical process faults (Dai and Zhao, 2011).

In Guzella et al. (2007), a Dynamic Effector Regulatory Algorithm was applied for fault and anomaly detection in case of a sugar factory from Poland. Other applications are: chemical sensor drift mitigation (Martinelli et al., 2013), charge state assignment of small molecule mass spectra (Kilgour et al., 2012).

The real-life case study considered for this work is represented by the separation of succinic acid from the fermentation broths. Succinic acid, a water soluble, colorless crystal is emerging as one of the most competitive new bio-based chemicals, its production from petroleum based products being replaced with renewable feedstock through a fermentation process. Due to the fermentation process, different chemical compounds are encountered in the broth, and therefore, a separation step must be performed. A set of anterior experiments indicated that separation of this acid by pertraction from the mixture obtained in fermentation is possible (Wang et al., 2010). But this process is difficult to perform and, to model because the inner workings are not fully know and understood. Consequently, the application of a CS optimized NN is an efficient way to model the system.

2. Clonal selection

Although based on different biological inspiration theories, the Clonal Selection and the Evolutionary Algorithms (EAs) are very similar because they are population-based search and optimize algorithms (Dasgupta and Nino, 2009). Also, the two central processes which are involved in antibodies production, genetic recombination and mutation, are the same as the ones used for the evolution of species reproduction. The same mechanism (that provides the variation on which natural selection is based) has the role of fitting the organism into the environment (de Castro and Von Zuben, 2000). Except for the inspiration source, the nomenclature, operators, and the specific adaptive mechanisms (Brownlee, 2007) represent other differences between CSs and EAs.

Multiple algorithms belonging to CS class can be encountered in literature, most of them having the same features (de Castro and Von Zuben, 2000): i) population initialization; ii) selection of the best individuals; iii) reproduction (cloning); iv) hyper-mutation of the clones and reselection of improved clones; and v) replacement of some of the antibodies from the population with novel ones (diversity introduction), operation which is called Receptor editing.

Initialization represents the first step of the algorithm, and it is recommended that the antibodies should be scattered uniformly over the feasible search space (Gong et al., 2010). The classical approach is represented by a random generation of antibodies (which are the B cells of the biological immune system (Cutello et al., 2004)) with a uniform distribution probability (Swain et al., 2011). In order to obtain better results, researchers applied a series of methods to improve the initialization step so that the search starts from a better pool of solutions (Dasgupta and Nino, 2009; Gong et al., 2010).

After that, the population is evaluated using affinity function. Each antibody has an associated affinity value, and, based on this information, some of them are selected for cloning. The affinity is computed using different measures, such as: crowding distance value (Chen et al., 2010), Euclidian distance (Zhang, 2011), and arithmetic expressions (Gan et al., 2009).

In the next step, a percent or a fixed number of the best affinity individuals are selected for cloning, which is the process of creating new antibodies from a single common ancestor (Chen et al., 2010). The number of clones is usually generated using one of the two principles: i) static cloning (a predefined number of clones is created for each selected antibody) and ii) proportional cloning (the number of clones is proportional to the antigenic affinities) (Cutello et al., 2004). After cloning, the clones are maturated, in order to improve their affinity. This is a process of variation and section achieved by somatic hyper-mutation (which performs the local search) and selection of the better matched

antibodies (which performs the global search) (Dasgupta and Nino, 2009). The hyper-mutation operator explores the search space by introducing innovation in the potential solution population (Cutello et al., 2004). When considering the mutation potential, the following variants of hyper-mutation operators exists: static, proportional, inversely proportional, hyper-macromutation and hybridizations (Cutello et al., 2004). Concerning the modality of introducing the hyper-mutation, the variants are: somatic hyper-mutation (Simoes and Costa, 2003), tangent vector (de Mello Honorio et al., 2007), Jacobian vector (de Mello Honorio et al., 2007), adaptive Gaussian (Goncalves et al., 2007), adaptive (Goncalves et al., 2007), two phase mutation process (Mobini et al., 2011).

After the clones are hyper-mutated, the affinity of the cloned population is computed, the individuals with the higher affinities being selected for introduction in the population.

3. hCS-NNm

The hCS-NNm algorithm proposed in this work is based on a previous CS-NN version (Dragoi et al., 2012), where CS is used to simultaneously optimize the topology and the inner parameters of the neural model. The parameters considered for optimization are: number of hidden layers, number of neurons in the hidden layers, weights, and bias, activation function and parameter of the activation function (whenever is the case). During the optimization, each neuron can have one of the following activation functions: Linear, Hard Limit, Bipolar Sigmoid, Logistic Sigmoid, Tangent Sigmoid, Sinus, Radial Basis and Triangular Basis. Another limitation imposed to the network is related to the number of hidden layers. As the majority of known processes can be modeled with a two hidden layer network, a limitation related to this parameter was set and each determined model can have none, one or two hidden layers.

As mentioned in the previous section, from a structural point of view, CS is similar to an EA, a set of potential solutions called antibodies being evolved through generations by the application of cloning, hyper-mutation, and receptor editing (similar to selection). A specific characteristic of the CS-NN algorithm is represented by a hybrid hyper-mutation approach in which one of the three types of hyper-mutation (Gaussian, non-uniform, and pair wise) is used, based on random parameter.

In its natural form, the NN cannot be optimized using CS, and therefore, an encoding procedure was applied to create a working inter-relation between the two algorithms. From the multitude of encoding approaches, a direct real value variant was chosen, not only for its simplicity, but also for the low computational cost it utilizes when performing encoding - decoding actions, at each iteration and for each antibody, at least one of this actions being performed.

As the antibodies used in CS-NN are representation of different NNs acting as models for the considered process, it is possible to include a back-propagation (BK) procedure as local search. The Random Search (RS) approach was alternatively applied to improve the best solution at the end of each generation because, during the evolution, the best solution may not change as often as desired and BK is helpful only when applied to a limited population (as it requires considerable computational resources when used for a high number of models). This combination of BK and RS applied as a local search procedure, along with its application in a real case study (which to the author's knowledge was never modelled with a clonal-neural approach) represents the novelty of this work.

A simplified schema of the proposed hCS-NNm algorithm, where stop condition is represented by the number of generations reaching a specific maximum limit, is presented in Fig. 1.

In this figure, *Nc* represents the number of individuals which will be cloned, *Ma* is the medium affinity of the population (computed as the average affinity of all the individuals from the population at the specific generation) and *bs* represents the best solution.

4. Database for the separation of succinic acid

The succinic acid, which is also known as amber acid or butandioic acid, is widely used in many areas, the production of this compound from renewable resources being more cost-effective than from petroleum based products (Song and Lee, 2006). Consequently, determining good succinate production hosts and optimal conditions which lead to maximum efficiency are problems which must be solved in order to obtain applicable workflows in large scale equipments.

Succinic acid is a dicarboxylic acid with numerous applications in chemical industry (reagents, synthetic resins, biodegradable polymers, electroplating, green solvents, detergents, inks), agriculture (pesticides, growth regulators and stimulators), pharmaceutical and food industries (amino acids, antibiotics, vitamins, surfactants, additives) (Liu et al., 2008; Song and Lee, 2006; Zeikus et al., 1999).

This acid is industrially produced using liquefied petroleum gas, namely butane, by chemical synthesis *via* maleic anhydride. The cost of this technology varies between 4.1 to 6.3 EUROs kg^{-1} succinic acid, depending on the acid's final purity, the contribution of raw materials to this cost being of 1 EURO kg^{-1} succinic acid (Song and Lee, 2006; Zeikus et al., 1999). Due to the difficulties of the chemical synthesis, succinic acid production by fermentation of *Actinobacillus succinogenes* or *Actinobacillus succiniproducens* have been considered as important alternative (Corona-Gonzalez et al., 2008; Dorado et al., 2009; Galaction et al., 2012; Li et al., 2010).

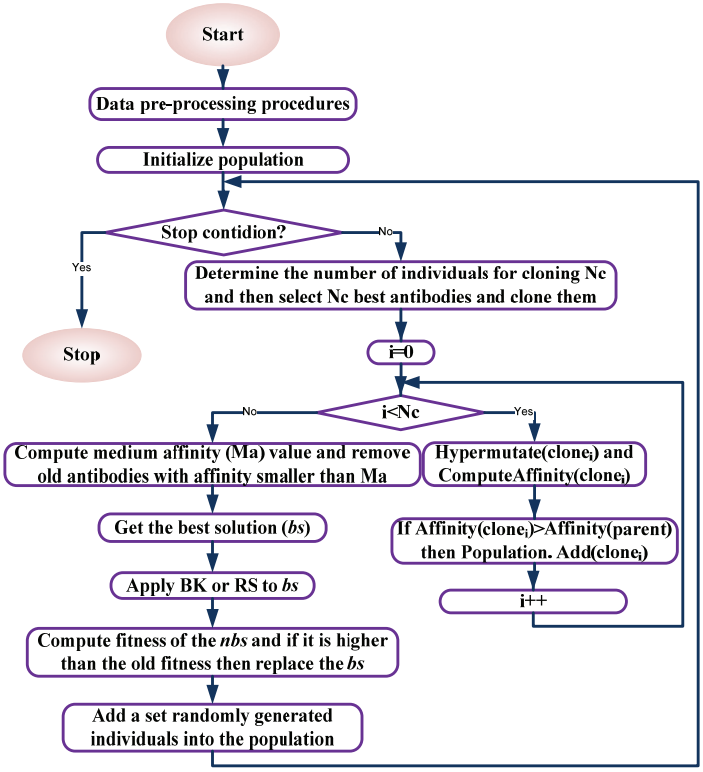

Fig. 1. The simplified schema of the hCS-NNm algorithm

However, the separation of succinic acid from the fermentation broths is difficult, especially due to the presence of other carboxylic acids, the most important being formic and acetic acids.

A series of previous experiments indicated that the selective separation of these acids by facilitated pertraction with tri-n-octylamine (TOA) of formic, acetic and succinic acid from their mixture obtained by *A. succinogenes* fermentation is possible (Galaction et al., 2013). Thus, formic and acetic acids can be transferred from the feed phase through liquid membrane to the stripping phase, while succinic acid remains in the feed phase. Superior values of selectivity factors can be obtained by combining the effects of pH-gradient between the aqueous phases, carrier concentration and mixing intensity on pertraction of carboxylic acids obtained by succinic acid fermentation.

In this context, the aim of applying a neural network optimizer as Clonal Selection is to establish the model describing the influences of the considered parameters on the pertraction selectivity. In the same time, the goal of the optimization is to find the operating conditions corresponding to the maximum selectivity factor.

The database used for modelling the separation of succinic acid from the fermentation broths is composed from experimental data. The experiments have been carried out using the pertraction equipment that allows obtaining and maintaining easily the solvent layer between the two aqueous phases (free liquid membrane).

The pertraction cell consists in a U-shaped glass pipe having an inner diameter of 45 mm and a total volume of 450 mL, the volume of each compartment being of 150 ml (Galaction et al., 2008). The aqueous solutions and the solvent phase have been independently mixed by means of double blade impellers with 6 mm diameter and 3 mm height. For the two aqueous phases, the rotation speed of the impellers varied between 0 and 800 rpm. The membrane phase has been mixed at 500 rpm. The area of mass transfer surface, both for extraction and for re-extraction, was of 1.59 x 10^{-3} m^2. The interfaces between the phases remained flat, and, hence, the interfacial area constant, for entire rotation speed domain used.

The experiments have been carried out in a pseudosteady-state regime, at steady-state conditions related to the aqueous phases and unsteady-state mode related to the membrane phase. The aqueous solutions have been separately fed with a volumetric flow of 2.5 L h^{-1}. The liquid membrane phase consisted of dichloromethane in which has been separately dissolved the carrier TOA, its concentration varying between 5 and 300 g L^{-1} (0.014 - 0.85 M).

The feed phases were aqueous solutions respecting the composition obtained by succinic fermentation with *A. succinogenes*: 33 g L^{-1} (0.28 M) succinic acid, 4 g L^{-1} (0.087 M) formic acid and 10 g L^{-1} (0.17 M) acetic acid, respectively (Dorado et al., 2009). The pH-value of the feed phase varied between 1 and 7, the pH adjustment being made with

solution of 3% sulfuric acid or 3% sodium hydroxide, function on the prescribed pH-value.

The stripping phases consisted of solutions of sodium hydroxide with pH = 7 - 12. The pH-values of both aqueous phases were determined using a digital pH-meter of Consort C836 type and have been recorded throughout each experiment. Any pH change was recorded during the extraction experiments.

The pertraction process was analyzed by means of the selectivity factor. For calculating this parameter, the acids concentrations in the feed and stripping phases have been measured and the mass balance for the pertraction system has been used. Succinic, formic, and acetic acids concentrations have been determined by high performance liquid chromatography technique (HPLC, Star Varian Chromatography Workstation) with a PL Hi-Plex H column (7.7 mm diameter, 300 mm length, 8 μm porous particle), provided with UV Prostar 330 PDA detector (Galaction et al., 2013). The mobile phase was a solution of 0.1% trifluoroacetic acid with a flow rate of 0.6 mL min^{-1}. The analysis has been carried out at 60°C.

A series of multiple experiments with varying parameters were performed, the final database having a set of 2370 data. For modeling purpose, 75% of data was used in the training phase and 25% in the testing phase. In addition, a normalization procedure was applied, to reduce the difference between the maximum and minimum values of each parameter.

4. Results and discussion

After data describing, the process was gathered and worked using a normalization procedure, various simulations with the hCS-NNm are performed in order to determine the algorithm's performance concerning model determination for the separation of succinic acid from mixtures of succinic, acetic, and formic acids formed in the fermentation broths. The main parameters considered for modelling the pertraction process were: pH value of feed phase (pHf), pH value of stripping phase (pHs), the TOA concentration (CTOA, g L^{-1}), and the impeller speed (N, rpm).

The architecture of the models (the CS work with) influences the computational resources. A direct dependency between how big the network is (in terms of number of hidden layer and neurons in each hidden layer) and the dimension of the corresponding encoding exists. Consequently, a set of limitation to the model architecture were imposed. For the majority of processes, it was observed that a network with a maximum of 2 hidden layers can provide acceptable results.

Therefore, a network modelling the separation of succinic acid from fermentation broths can have maximum 2 hidden layers. On what concerns the maximum number of neurons in the two hidden layers, a set of 30 and respectively 20 was considered sufficient.

A set of five best results obtained with the proposed hCS-NNm algorithm are presented in Table 1, where a 'inputs: no_neurons_first_layer: no_neurons_second_layer: ouputs' notation is used to represent the network topology. In order to determine the effectiveness of the proposed hCS-NNm algorithm, a comparison with an earlier version CS-NN (Dragoi et al., 2012) was performed. The best model determined with CS-NN had a topology of 4:8:1:1, with a mean squared error (of the normalized data) in the training phase of 0.0414 and of 0.0696 in the testing phase.

Also, the average relative error (ARE) for the best models obtained with the best algorithms were computed (Table 2). As it can be observed, after the data is de-normalized, the error in the training and testing phases are still lower for the hCS-NNm.

For a representative set from the training and testing data, a comparison between experimental data, predicted data with hCS-NNm and CS-NN is given in Figs. 2 and 3. As the curve of hCS-NNm is closer to the experimental data than the one of CS-NN, it was concluded that hCS-NNm works better.

Table 1. Results obtained with the hCS-NNm algorithm

Neural network topology	*Training mean squared error*	*Testing mean squared error*
4:16:2:1	0.0405	0.0601
4:10:1	0.0409	0.0662
4:29:3:1	0.0430	0.0686
4:29:1	0.0431	0.0601
4:15:10:1	0.0445	0.0702

Table 2. The average relative error for the best models

Algorithm	*Model*	*Training ARE*	*Testing ARE*
hCS-NNm	4:16:2:1	14.59%	15.04%
CS-NN	4:8:1:1	30.87%	36.73%

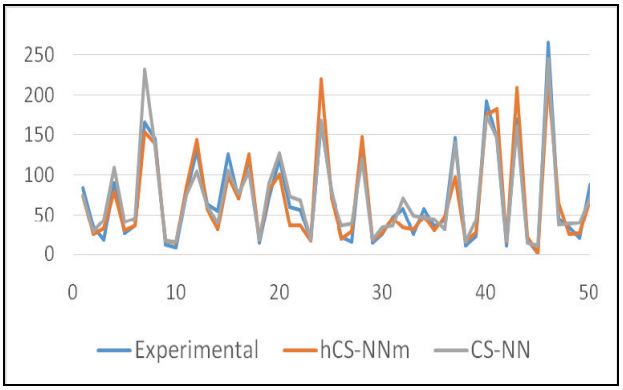

Fig. 2. Expected and neural network predictions for a representative set from the training data

5. Conclusions

In this work, the successful modelling of the succinic acid separation from fermentation broths was performed using a new hybrid combination of ANNs, CS, BK, and RS, called hCS-NNm.

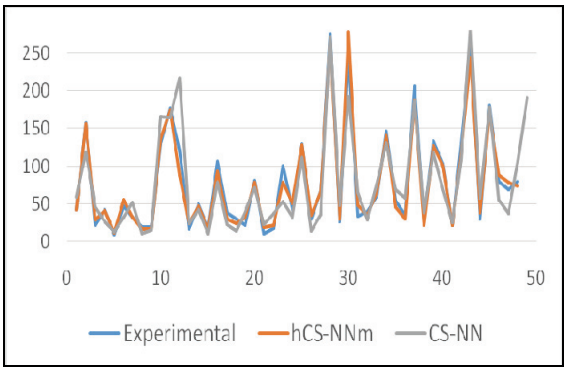

Fig. 3. Expected and neural network predictions for a representative set from the testing data

In this combination, ANN modeled the process, while the CS is the optimizer used to modify the model's parameters in order to minimize the error between predicted and experimental data.

In addition, BK and RS were applied (based on a random number generator) for the improvement of the best solution found so far. In this manner, the performance was further improved, as it was demonstrated by the application of hCS-NNm for modelling the succinic acid separation from fermentation broths, where it proved to be an efficient and reliable tool.

Acknowledgments

This work was supported by the "Partnership in priority areas – PN-II" program, financed by ANCS, CNDI - UEFISCDI, project No. 23/2012.

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