

# Model-based Derivation of the Safety Operating Limits of a Semi-batch Reactor for the Catalytic Acetoacetylation of Pyrrole Using a Generalized Sensitivity Criterion

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The safe operation of a semi-batch catalytic reactor remains a sensitive issue when highly exothermic side reactions may occur, and various elements such as controllability, stability, safety, and economic aspects have to be considered in the process development. Nominal operating conditions are set to avoid excessive thermal sensitivity to variations in the process parameters. Several shortcuts or model-based methods are used to estimate the safety limits and runaway boundaries for the operating variables. Among them, the Morbidelli & Varma (MV) generalized sensitivity criterion proved to be a powerful method for assessing the critical conditions of a chemical process. The approached case study concerns a semi-batch reactor used for the acetoacetylation of pyrrole with diketene in homogeneous liquid phase. The catalytic process is known to be of high risk because of the very exothermic side-reactions involving reactive diketene and, as a consequence, it requires rigorous control of the operating parameters. Previous studies tried to maximize the isothermal reactor performances by using various optimal feeding policies of the co-reactant under semi-empirically derived safety constraints. The present work illustrates how the runaway critical conditions can be precisely assessed and the safe operating region well established based on an extensive safety analysis and an adequate process model of reduced complexity. In addition, by screening the influential variables, the study also proves the close connection between the operating safety limits and the process kinetics/thermodynamics, initial/inlet and cooling conditions, offering a better support for the reactor optimization.

*Key words:*

Runaway conditions, semi-batch reactor, generalized sensitivity, pyrrole, diketene

## Introduction

Batch and semi-batch processes are of considerable importance in the fine chemical and biochemical industry, a large variety of specialty chemicals, pharmaceutical products, and polymers being produced at a small or large scale. The optimization efforts are primarily focused on the reactor because of the high value of raw materials and products, but also because of its high sensitivity to operating conditions, and risk. Due to the implicit reactor dynamics, such processes are usually conducted following optimal operating policies and using a tight control to prevent loss of production due to variability of the process conditions. Undesirable variations in raw materials, catalyst characteristics, recycle conditions, or operating parameters, all require a continuous adaptation of the process monitoring. Consequently, an advanced control is usually implemented in order to keep the reaction synthesis within defined safety limits and in an economic operating region.<sup>1</sup>

However, operating conditions that change from batch to batch may result in unacceptable variations of the product quality, additional operations for process corrections, or worse, the loss of the batch.<sup>2</sup> Besides, safety problems also have to be reconsidered every time: only in the EU, the statistics report runaway for ca. 10–15 % of batch (BR) or semi-batch (SBR) reactors annually.<sup>3</sup> Therefore, separate supervision of each BR or SBR, and periodical updates of the safety margins for the operating variables based on a process model become necessary. Such a procedure involves an initial on-/off-line data analysis in order to obtain the primary information on the process (estimation), a subsequent (model-based) optimal control using the previous information, and an optimization procedure applied under known technological constraints. The dynamic optimization accounting for process uncertainty has been extensively approached in the dedicated literature due to its significant impact in industry and process system engineering including design, identification, control, estimation, production scheduling and planning.<sup>4,5</sup>

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Most of the previous researches on batch and semi-batch processes were rather focused on finding optimal operating policies leading to maximization of a performance criterion on a cost basis (productivity, batch time) by using an efficient optimization problem solver.<sup>4,6–10</sup> Safety operation indices are accounted rather as constraints or parameter thresholds and seldom integrated in the optimization objective function, with or without accounting for process uncertainty.<sup>11–14</sup> A hierarchical optimization can be applied by ranking economic, sensitivity (thermal risk), and eventually environmental objectives according to their importance, and then trying to solve the problem in successive steps by imposing restrictions that maintain the solution within the optimal region previously determined.<sup>15</sup> Alternatives also consider cost optimization under safety constraints by imposing system failure probability thresholds, or sensitivity objectives under technological constraints and imposing thresholds for an acceptable cost with/without considering uncertainty in model or parameters.<sup>4,6,13,16,17</sup> Often when conducting highly exothermic reactions, safety considerations encourage a conservative, under-optimal operational strategy of the SBR in order to prevent accumulation of co-reactant in the vessel as a result of an inappropriate temperature policy in the reactor, leading to possible runaways at higher temperatures.<sup>5,18</sup>

In all alternatives, accurate evaluation of the safe operating region that exhibits low sensitivities, by setting the runaway boundaries in the parametric space, represents the crucial step. Model-based calculation of such limits is not an easy task, not only because of the computative numerical algorithms to be applied, but also due to fluctuations in the characteristics of the process, catalyst, impurities, and raw-materials, thus requiring periodic model updating (of known reaction pathway),<sup>2,19,20</sup> and consequently an update of the runaway boundaries themselves.

In practice, the process safety limits are many times determined from experimental observations on the system thermal sensitivity under known reactor configuration, or from operation experience with similar processes. Simple engineering numbers, such as Damköhler or Stanton, or safety indices may give an approximate idea on the safety limits and many times replace the systematic model-based safety analysis of the process.<sup>21,22</sup> Parametric sensitivity of semi-batch reactors is also a well-studied aspect of the safety analysis. The large number of influencing variables, and the (catalytic) kinetics complexity makes the detailed thermal sensitivity analysis difficult, and therefore justifies the development of a quite large number of methods intended to establish the safety limits for

the operating variables. The complexity of these methods depends on the available information about the process kinetics, thermodynamics, reaction pathway, being individualized for every type of reactor (e.g. geometry-based, sensitivity-based, or explicit methods; see reviews of Varma *et al.*,<sup>23</sup> Maria,<sup>22</sup> Stoessel,<sup>24</sup> Maria and Stefan<sup>25</sup>). Advances in experimental techniques for on-line data acquisition allow a quick process model updating and, subsequently, re-calculation of the safety limits under variable feeding/operating parameters.

The scope of this paper is to illustrate how the runaway operating boundaries of a SBR can be established and up-dated by using a generalized sensitivity criterion and an adequate process model of relative low complexity. The method allows to point-out the operating regions of high thermal sensitivity, while the process sensitivity functions can be further used to determine the optimal operating conditions and the control policy that meet the productivity and safety requirements.<sup>2</sup> The safe operating region depends not only on the system geometry and flow conditions but also more strongly on the chemical process itself. When new data are available, runaway boundaries must be re-calculated and included as process constraints during the optimal control.

An example is provided in the case of a bench-scale homogeneous semi-batch reactor for catalytic acetoacetylation of pyrrole with diketene in homogeneous liquid phase. Previous studies investigated the on-line optimization of the reactor by using various feeding policies. The present work is focused on quantitatively assessing the hazard arising from very exothermic side reactions by using several risk indices, and a model-based sensitivity analysis intended to set the critical inlet/operating conditions leading to process runaway. By screening the influential variables, the study also proves the close connection between the operating safety limits and the process kinetics/thermodynamics, flow and cooling conditions.

## Semi-batch process hazard assessment – A short review of theoretical aspects

A chemical reaction with a high heat effect is preferably conducted in a semi-batch mode: one of the reactants is slowly added to the second component, which has already been fully loaded to the reactor. Thus, the evolution of the reactor temperature can be kept under control, while a certain feeding policy can ensure production maximization.

Runaway and eventual explosion of a SBR may occur when the rate of heat generation becomes faster than the rate of heat removal by the

cooling system. In the homogeneous reaction case, the accumulation of the co-reactant is possible at low temperatures due to the reduced reaction rates. Consequently, a sudden increase in the reaction temperature leads to an exponential rise in the reaction rates (when co-reactants are in large amounts), which in turn will lead to a continuous rise in the reactor temperature up to conditions when the cooling system becomes ineffective, eventually determining the reactor explosion. The situation is worsened by the occurrence of exothermic chain/polymerisation reactions that lead to a quick increase in temperature or pressure with eventually the same effect.<sup>21,23,24</sup> In the heterogeneous liquid-liquid systems, runaway usually occurs for slow reactions, when mass transfer is not yet enhanced by chemical reaction. Low reaction temperatures, low mass transfer rates, and insufficient interfacial areas between the two phases may lead to co-reactant accumulation which, under certain operating conditions, may lead to reactor runaway.<sup>3</sup> Even if rarely, runaway in heterogeneous SBR can also occur for rapid reactions, when the rapid co-reactant is consumed in the boundary layer, but it may accumulate in its own phase.

In both homogeneous and heterogeneous SBR cases, approximate boundary line diagrams in the operating parameter planes can be obtained by using simple engineering numbers for simple reaction kinetics, thus separating regions with conditions where the reactions are sufficiently fast and with conditions where runaway may occur.<sup>3,26</sup>

More systematically, the hazard assessment of the process and plant is usually structured on four levels, as described by the SREST method (Substance, Reactivity, Equipment and Safe-Technology Layers).<sup>27,28</sup>

i) Substance risk assessment (SAL) is based on safety indices of involved species concerning the mobility in the environment, fire/explosion danger, reactivity/decomposition characteristics, acute toxicity, danger for health (skin irritation, chronic toxicity), effects on environment (bioaccumulation, solid waste, biodegradability), amended by a certain pollutant fate index.<sup>29</sup>

ii) Reactivity assessment (RAL) is based on reaction safety indices such as: reaction heat ( $-\Delta_r H$ ), overall kinetics ( $A, E$ ) (determined by calorimetric means and correlation methods of kinetic data),<sup>21,30–33</sup> severity indices such as the adiabatic temperature rise ( $\Delta T_{ad}$ ),<sup>34</sup> probability indices such as the time-to-maximum-rate under adiabatic conditions ( $TMR_{ad}$ ) and S-index,<sup>31</sup> temperature for adiabatic decomposition in 24 h ( $ADT_{24}$ ),<sup>21</sup> reaction type, reaction violence index ( $B$ ),<sup>21</sup> RHI index,<sup>35</sup>

NFPA  $N_R$ -index, incompatibility of compounds and chemical interactions, etc.:

$$TMR_{ad} = t|_{r=r_{max}}; \quad \Delta T_{ad} = (-\Delta_r H)c_{j,0}/(\bar{\rho}\bar{c}_p);$$

$$B = \Delta T_{ad}E/(RT_0^2), \quad (1)$$

(where:  $c_{j,0}$  = initial concentration of key species;  $\bar{\rho}$  = reacting mixture density;  $\bar{c}_p$  = average specific heat capacity;  $T_0$  = initial temperature of the reaction;  $R$  = universal gas constant;  $t$  = reaction time). Values of  $(-\Delta_r H) > 50 \text{ kJ mol}^{-1}$ ,  $TMR_{ad} < 8 \text{ h}$ ,  $\Delta T_{ad} > 50 \text{ K}$ , and  $B > 5$  indicate potentially dangerous reactions,<sup>21</sup> presenting a fast evolution and significant exothermicity. According to Grever,<sup>21</sup> the analysis can be applied for both primary (desired) and secondary (undesirable) reactions by means of simple but practical tests under adiabatic or non-adiabatic conditions. For simple reactions, the approximate empirical critical operating conditions depend on  $ADT_{24}$  and  $T_{onset}$ , indices that can be deduced from dual scanning calorimetric measurements. More elaborated reaction hazard indices, such as IC of Shah *et al.*,<sup>27</sup> try to correlate several risk indices and interactions between primary and secondary reactions.

iii) Equipment safety assessment (EAL) is based on runaway scenarios (as probability and severity) in reactors, storage tanks, distillation columns, dryers, etc. In order to evaluate the consequences of accidents (vapour cloud, toxic release, fire/explosion, runaway) caused by reaction exothermicity and dangerous substances, classical chemical process quantitative risk analysis (CPQRA)<sup>36</sup> is applied. Simplest approach for evaluating the safety operating limits does not use a mechanistic model for the reactor or for the process, but uses only the past experience stored in databanks concerning compounds properties and safety aspects of the involved reactions and equipment.

iv) Safety technology assessment (STAL) is based on a combination of scores (hazard indices) assigned in the preliminary SAL, RAL, and EAL analysis steps. Multiple nomograms are used to score the risk at each safety analysis level. The rule ends with suggesting further technology improvements, each action being associated with a risk reduction factor in order to get the overall hazard indices of the plant below some suggested thresholds.<sup>27,28</sup>

Regarding the reactor, simple but approximate methods can indicate risky conditions for every type of reactor by using safety indices based on engineering numbers. For a SBR it is important to investigate not only how fast and exothermic the dangerous reaction is, but also the relation with the rate

of addition of the co-reactant. By using engineering numbers, critical conditions for homogeneous reactions of  $n$ -th order are given by:<sup>21,24</sup>

$$Da = \frac{\tau_D}{\tau_1} = \frac{(-\nu_A)r_A\tau_D}{c_{A,0}} < 50 - 100,$$

(slow reactions vs. addition time);

$$Da/St < 1; \quad St = \frac{UA_r\tau_D}{V\bar{\rho}\bar{c}_p}, \quad (2)$$

(where:  $\tau_D$  = time of addition of the co-reactant;  $\tau_1$  = reaction time constant, e.g.  $1/(k_0c_{B,0})$  for the 2-nd order reaction between A and B at small conversions;  $k_0$  = reaction rate constant at the cooling temperature;  $U$  = heat transfer coefficient;  $A_r$  = heat transfer area;  $V$  = reactor volume;  $Da$  = Damköhler number for the key reactant A (start material);  $St$  = Stanton number;  $(-\nu_A)$  = stoichiometric coefficient of reactant A). A slow reaction, of average reaction time constant  $\tau = 1/k_0$  smaller than the co-reactant adding time  $\tau_D$  (i.e. small  $Da$  numbers), can become very dangerous because of the accumulated un-reacted components at low temperatures. The subsequent increase in temperature to start-up the reaction will lead to a sudden increase in the reaction rate and temperature, which cannot be prevented by strong cooling, eventually leading to reactor explosion. Such a simple check will also be used in the present work. For heterogeneous SBR, similar runaway conditions can be derived by accounting for the so-called Exothermicity, Reactivity, and Cooling numbers, that combine influences of various operating parameters leading to operation within a critical region.<sup>3</sup>

The cooling systems are usually designed to efficiently remove the primary reaction heat, and often become ineffective when highly exothermic secondary reactions occur. Thus, establishment of critical operating conditions and runaway boundaries become crucial for the safe operation of the process. For instance, for a single irreversible reaction, the critical difference between the batch reactor temperature ( $T$ ) and the cooling agent temperature ( $T_a$ ) should not exceed  $\Delta T_c = (T - T_a)_c = RT^2/E$ , according to the Semenov theory. For a zero-order reaction the critical BR condition corresponds to  $\Delta T_c = (T - T_0)_c = RT_0^2/E$ , while the critical conversion to  $X_c = \Delta T_c/\Delta T_{ad} \approx 1/B$ .<sup>21</sup>

*Explicit criteria* have been elaborated to quickly define critical operation conditions for each reactor type by means of simple and explicit semi-empirical relationships, and thus avoiding the solution of complicated (homogeneous or heterogeneous) reactor models and fulfillment of implicit runaway conditions (review of Varma *et al.*<sup>23</sup>).

However, such semi-empirical calculations are imprecise and difficult to be applied in the case of a complex reaction pathway. This is why a kinetic *model based analysis* can lead to an accurate safety assessment for every reactor type, with a detailing degree depending on the model complexity and utilization scope. For the BR and SBR, two categories of model-based methods are mentioned (review of Varma *et al.*<sup>23</sup>): geometry-based methods and sensitivity-based methods.

*Geometry-based methods* interpret the shape of the axial temperature or heat-release rate profile over the batch time. The critical runaway conditions correspond to a high thermal sensitivity of the reactor and to an accelerated temperature increase, which in a temperature – time plot  $T(t)$ , corresponds to an inflexion point before the curve maximum. The same criterion is valid if the abscissa is replaced by the key-reactant conversion ( $X$ ). Based on several necessary and sufficient conditions, various alternatives are proposed in order to predict the critical operation in the parameter space ( $c_{A,0}$ ,  $c_{D,in}$ ,  $T_0$ ,  $T_a$ ,  $Q_D$ , where index ‘A’ refers to the reactant, ‘D’ to the continuously added co-reactant). By denoting with  $q_G$  and  $q_T$  the generated and released heat fluxes in the energy differential balance, the main runaway criteria are: the Semenov criterion (requiring  $q_G = q_T$  and  $\partial q_G/\partial T = \partial q_T/\partial T$  conditions to be fulfilled at the critical point); the Thomas & Bowes criterion (based on  $\partial^2 T/\partial t^2 = \partial^3 T/\partial t^3 = 0$  conditions); the Adler & Enig criterion (based on  $\partial^2 T/\partial X^2 = \partial^3 T/\partial X^3 = 0$  conditions); the van Welsenaere & Froment criterion (based on  $\partial X^*/\partial T_{max} = 0$  condition, where  $X^*$  is the conversion at the maximum temperature  $T_{max}$ ).

*Sensitivity-based methods* explicitly introduce the concept of parametric sensitivity of a state variable  $y$  with respect to a parameter  $\phi$ , i.e.:

$$s(y; \phi) = \partial y/\partial \phi,$$

(absolute sensitivity coefficients);

$$S(y; \phi) = (\phi^*/y^*)s(y; \phi),$$

(relative sensitivity coefficients); (3)

(where  $\phi^*$  = nominal operating point in the parameter space). Unsafe conditions correspond to sensitive operating points when “the reactor performance becomes unreliable and changes sharply with small variations in parameters”.<sup>23</sup> The dependence of the state sensitivity (i.e. temperature, conversion, selectivity, species concentrations, pressure) on the process parameters is computed by means of a sensitivity differential equation solved simultaneously with

the reactor mass, heat and momentum balance equations. The runaway analysis can be developed for every state variable vs. every parameter in the so-called *local sensitivity analysis* leading to local runaway conditions of the reactor. Of higher interest are the sensitivities at the beginning of the batch process. If calculations are extended over the whole batch operation time, by accounting for concomitant variations of several input/process parameters, the analysis is called *global sensitivity analysis* leading to global runaway conditions for the reactor.

A common way to determine the critical operating conditions for a BR or SBR is to compute the time dependent sensitivity functions  $s(y; \phi)_t = \partial y(t)/\partial \phi$  by using the direct differential method and sensitivity equations:<sup>14,23,37</sup>

$$\frac{ds(y; \phi_j)}{dt} = \frac{\partial g}{\partial y} s(y; \phi_j) + \frac{\partial g}{\partial \phi_j}; \quad (4)$$

$$s(y; \phi_j) \Big|_{t=0} = \delta(\phi_j - y_i),$$

where the Kronecker delta function  $\delta(\phi_j - y_i)$  takes the value 0 (for  $\phi_j \neq y_i$ ) or 1 (for  $\phi_j = y_i$ ). The sensitivity equations must be integrated simultaneously with the reactor model:

$$dy/dt = g(y, \phi, t), \quad y(0) = y_0. \quad (5)$$

Among the process parameters, one can mention the initial or input conditions, or reaction characteristics, i.e.  $\phi_j = [T_0, T_a, c_{j,0}, c_{j,in}, p_0, B, U, \dots]$  However, of most interest is the local sensitivity of the reactor temperature hot-spot  $\Delta T_{peak} = (T_{max} - T_0)$  or  $T_{max}$  reached during the batch operation. Detection of the operating regions where certain combinations of parameters lead to a high thermal sensitivity of the SBR offers the possibility to accurately set the safety limits of the operating region.

For simple process models, evaluation of derivatives in (4) can be performed analytically. However, such a direct procedure is difficult to be applied for complex kinetic/reactor models with implicit terms. Difficulties also appear when a rapid kinetics induces system stiffness that increases numerical problems when simultaneously solving the model and sensitivity equations. For such cases, the numerical finite difference method (FDM), also used in the present study, is a worthy alternative. However, it should be mentioned that an accurate evaluation of high sensitivities of state variables with FDM is computational costly when approaching the runaway boundaries because it requires small discretization steps in the parameter space.

A generalized sensitivity criterion of thermal runaway is offered by Morbidelli and Varma

(MV).<sup>23</sup> According to the MV criterion, the hot spot ( $T_{max} - T_0$ ) induces a sharp increase of the normalized sensitivity  $S(T_{max}; \phi)$  under critical conditions, independently of the considered operating parameter (e.g.  $T_0, c_{j,0}, Q_{in}, T_a, B, Da, St, \dots$ , or a combination of them). Thus, the critical conditions correspond to the maximum of the absolute value of the maximum-temperature sensitivity with respect to a certain parameter  $\phi$ , i.e. to the maximal values of  $|s(T_{max}; \phi)|$  or  $|S(T_{max}; \phi)|$ .

A convenient alternative to (4) is to use the Green's function method, suitable when the number of reactions is much larger than that of the considered species in the kinetic model.<sup>23</sup> The Green's functions  $G_{ij} = \partial x_i(t)/\partial x_{i,0}$  are in fact the sensitivities of the state variables  $x$  to the initial conditions, also accounted by the MV criterion. The time-dependent Green's function matrix  $G = [G_{ij}]$  can be evaluated from the model linearization, by using the differential equation integrated simultaneously with the reactor model:<sup>38</sup>

$$dG/dt = J(x(t))G, \quad G(0) = 1, \quad J = \partial g/\partial x, \quad (6)$$

$$dx/dt = g(x, \phi, t), \quad x(0) = x_0.$$

Finally, it should be noted that most of the mentioned runaway criteria are particularized for the case of an irreversible first- or  $n$ -th reaction order, leading to a simpler runaway problem treatment. In contrast, a generalized sensitivity approach such as the MV criterion is applicable also to complex reactions.

Regardless of the method used, the safety analysis of the semi-batch catalytic reactors is still of high interest due to the variability in operating conditions inducing non-linear behaviours of complex processes and the requirement to optimize the reactor operation when the catalyst or raw-material properties change, or when the productivity has to be increased by operating the reactor in the vicinity of the safety limits. On the other hand, the chosen nominal operating point tries to limit the hot spot during the batch, avoiding an excessive sensitivity to variations in the process parameters.

## Process kinetics, reaction risk, and semi-batch reactor model

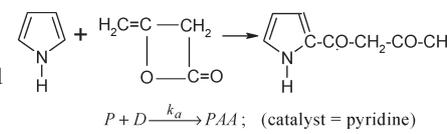
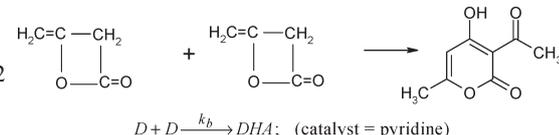
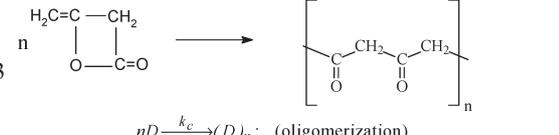
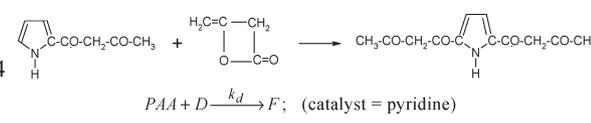
The acetoacetylation of pyrrole with diketene in homogeneous liquid phase, having pyridine as catalyst, is a common method for producing pyrrole derivatives (such as PAA = 2-acetoacetyl pyrrole) useful in the drug industry.<sup>39,40</sup> The process is known to be of high thermal risk due to the tendency of very reactive diketene to polymerise at higher tempera-

tures, or in the presence of impurities that can initiate exothermic side reactions difficult to be controlled.<sup>41</sup> A few number of investigations on the process kinetics have been reported, the most relevant being the study of Ruppen *et al.*<sup>2</sup> in a semi-batch isothermal reactor operated at 50 °C and normal pressure in a high excess of toluene as solvent. Although optimal catalyst load and temperature can be determined from separate lab-scale experiments, operation of the industrial SBR is difficult. Small variations in the catalyst/raw-material/solvent quality, a sudden increase in temperature, or an accumulation of reactive diketene favour secondary reactions that significantly change the selectivity between the desired and undesired products, and therefore lead to significant variations in the product quality from batch to batch.

The process main reactions are given in Table 1. The synthesis of the desired PAA product is accompanied by several side-reactions of diketene, leading to the dimmer DHA, oligomers  $D_n$ , or PAA derivatives denoted by F (the intermediate reaction of diketene with DHA has been neglected from the model). The co-reactant diketene is known to present an extreme reactivity and hazardous properties, as revealed by existing databases (the lower explosion limit in atmosphere being  $\varphi = 2.5$  %).<sup>42</sup> Because of that, the temperature regime must be strictly controlled and diketene concentration in the reactor kept lower than a certain critical threshold (ca. 0.025 mol L<sup>-1</sup>, empirically determined).<sup>43</sup>

The reactions are considered to be of first or second order, with the rate constants evaluated by Ruppen *et al.*<sup>2</sup> at nominal operating conditions

Table 1 – Process main reactions, proposed kinetic model,<sup>2</sup> and assessment of reaction hazard potential.<sup>21,22</sup>  
Notations: D = diketene; P = pyrrole; PAA = 2-acetoacetyl pyrrole; DHA = dehydroacetic acid.

#	Chemical reaction	Rate expression	Rate constants (Note a)	Reaction enthalpy (Note b)	$\Delta T_{ad}$ (Note c)	$TMR_{ad}$ (Note d)	B index (Note e)
1	 $P + D \xrightarrow{k_a} PAA$ ; (catalyst = pyridine)	$r_a = k_a c_P c_D$	$A_a = 3.1324 \cdot 10^{12}$ $L \text{ mol}^{-1} \text{ min}^{-1}$ $E_a/R = 10242.4 \text{ K}$	$\Delta_r H_a = -132.69$ $\text{kJ (mol P)}^{-1}$	61.8 K	3.57 min	6.07
2	 $D + D \xrightarrow{k_b} DHA$ ; (catalyst = pyridine)	$r_b = k_b c_D^2$	$A_b = 7.5651 \cdot 10^{12}$ $L \text{ mol}^{-1} \text{ min}^{-1}$ $E_b/R = 10242.4 \text{ K}$	$\Delta_r H_b = -91.92$ $\text{kJ (mol D)}^{-1}$	5.3 K	3.95 min	0.52
3	 $nD \xrightarrow{k_c} (D)_n$ ; (oligomerization)	$r_c = k_c c_D^n$	$A_c = 1.6549 \cdot 10^{12}$ $\text{min}^{-1}$ $E_c/R = 10242.4 \text{ K}$	$\Delta_r H_c = -1426.12$ $\text{kJ (mol D)}^{-1}$	83.0 K	4.75 min	8.15
4	 $PAA + D \xrightarrow{k_d} F$ ; (catalyst = pyridine)	$r_d = k_d c_{PAA} c_D$	$A_d = 1.7731 \cdot 10^{12}$ $L \text{ mol}^{-1} \text{ min}^{-1}$ $E_d/R = 10242.4 \text{ K}$	$\Delta_r H_d = -132.69$ $\text{kJ (mol PAA)}^{-1}$	7.7 K	4.21 min	0.76

(a) Arrhenius correlations of type:  $k = A \cdot \exp(-E/RT)$ ;  $R$  = universal gas constant;  $E$  = activation energy ( $E/R$  in K);  $A$  = frequency factor. Lacking of kinetic data, the activation energy has been adopted the same for all reactions, corresponding to those of diketene derivate polymerization;<sup>44</sup> the adopted values are in the same range with the free-radical polymerization of olefins.<sup>45</sup> Rate constants at 50 °C are:<sup>47</sup>  $k_a = 0.053$ ;  $k_b = 0.128$ ;  $k_c = 0.028$ ;  $k_d = 0.003$  (all in  $L \text{ mol}^{-1} \text{ min}^{-1}$ , except  $k_c$  in  $\text{min}^{-1}$ ). Rate constants increase also with the medium polarity (not accounted here), the reported values being valid for  $[PAA] > 0.1 \text{ mol L}^{-1}$ .<sup>2</sup> Other secondary reactions (such as  $DHA + D \rightarrow G$ ) have been neglected.

(b) Heat of reaction #1 has been determined from species standard molar enthalpies of formation  $\Delta H_f^0$ .<sup>54</sup> Heat of reaction #2 has been taken from the report of Lopatin *et al.*<sup>55</sup> Heat of reaction #3 has been determined by using the standard  $\Delta H_f^0$  of diketene oligomer  $D_n$ , of  $\Delta H_f^0 = -3756.9 \text{ kJ mol}^{-1}$ , corresponding to a  $n = 10$  cyclic oligomer or a  $n = 12$  acyclic,<sup>41</sup> and according to the Joback formula:<sup>53</sup>  $\Delta H_f^0 = 68.29 + \sum s_i I_{H_i}$  ( $\text{kJ mol}^{-1}$ ), where  $s_i$  = the number of structural groups of type  $i$ ;  $I_{H_i}$  = the increments of structural groups  $i$  for enthalpy of formation. Heat of reaction #4 has been adopted the same with those of reaction #1.

(c)  $\Delta T_{ad}$  = temperature rise under adiabatic conditions, computed for each reaction with the formula:<sup>46</sup>  $\Delta T_{ad} = (-\Delta_r H) c_{j,0} / (\rho_l c_{p,l})$ , where  $c_{j,0}$  = initial concentration of key species (see nominal values in Table 2);  $\rho_l$  = liquid mixture density;  $c_{p,l}$  = specific heat capacity of the liquid mixture.

(d)  $TMR_{ad}$  = time-to-maximum-rate under adiabatic conditions, obtained by simulations with the semi-batch reactor.

(e)  $B = \Delta T_{ad} E / (RT_0^2)$  = reaction violence index,<sup>21</sup> where:  $T_0$  = initial temperature of the reaction. A value of  $B > 5$  indicates a dangerous reaction with a high potential for thermal explosion.

around 50 °C, small quantities of pyridine, and PAA concentrations higher than 0.1 mol L<sup>-1</sup>. Due to incomplete kinetic data, an activation energy of  $E/R = 10242$  K was adopted for all reactions of diketene, by analogy with the diketene derivate polymerization<sup>44</sup> and with the initiation energy of olefin polymerization.<sup>45</sup> The resulted Arrhenius constants are displayed in Table 1. When additional kinetic information will become available, more precise values for activation energies will offer the possibility to refine the model solution without any modification in

the risk assessment methodology. All reactions are moderately exothermic, except for the highly exothermic diketene oligomerization of standard heat around  $-1423$  kJ mol<sup>-1</sup> (for a  $n = 10$ – $12$  degree of oligomerization, see footnote of Table 1).

Based on these data, one can a-priori assess the reaction hazard by computing  $TMR_{ad}$ ,  $\Delta T_{ad}$ , and  $B$  indices with formula (1), at nominal operating conditions presented in Table 2. The resulted values are (Table 1):  $TMR_{ad} \approx 4$  min (much smaller than 8 h);  $(Fc_{D,in})(t) = 62$  K (reaction #1) and  $\Delta T_{ad} = 83$  K (reaction #3) (i.e. larger than the threshold 50 K);  $B = 6$  (reaction #1) and

Table 2 – Reactor characteristics, nominal and recommended operating region<sup>2,48</sup>

Variable		value		
initial liquid volume		$V_0 = 1$ L		
reactor inner diameter		$d_r = 0.1$ m		
speed of the stirrer		$n = 640$ min <sup>-1</sup>		
liquid physical properties		toluene solvent		
Operating conditions <sup>43,47,48</sup>		minimum	nominal	maximum
inlet diketene concentration ( $c_{D,in}$ /mol L <sup>-1</sup> )		4–5	5.82	6
initial pyrrole concentration ( $c_{P,0}$ /mol L <sup>-1</sup> )		0.40	0.72	0.80
initial diketene concentration ( $c_{D,0}$ /mol L <sup>-1</sup> )		0.005–0.007	0.09	0.14
initial 2-acetoacetyl pyrrole concentration ( $c_{PAA,0}$ /mol L <sup>-1</sup> )		0.08–0.10	0.10	0.20
initial dehydroacetic acid concentration ( $c_{DHA,0}$ /mol L <sup>-1</sup> )		0.01–0.02	0.02	0.04
feed D solution flow-rate ( $Q$ /L min <sup>-1</sup> )		0.0005	0.0010–0.0015	0.0015
batch operating time ( $t_f$ /min)		145	150	186–300
initial temperature ( $T_0$ /°C)		40	50	60
feeding solution temperature ( $T_{in}$ /°C)		20	50	50
cooling agent average temperature ( $T_a$ /°C)		20	50	50
#	Process constraints:	Threshold	Observations	
1	PAA yield ( $\eta_{PAA}/\eta_{P0}$ )	0.583 (a)	productivity goal	
	PAA net yield ( $\eta_{PAA} - \eta_{PAA,0}/\eta_{P0}$ )	0.483 (a)		
2	final dehydroacetic acid concentration ( $c_{DHA}$ , mol L <sup>-1</sup> )	0.15 (a)	prevent precipitation of DHA at room temperature (solubility, at 50 °C is 0.20 mol L <sup>-1</sup> )	
3	final diketene concentration ( $c_D$ , mol L <sup>-1</sup> )	0.025 (a,b)	avoid high concentrations of this very toxic compound in the product mixture (a); also empirical critical runaway condition (b)	
4	Damköhler number ( $Da$ )	50–100 (c)	thermal safety critical index in semi-batch reactors for fast reactions	
5	Damköhler/Stanton number ( $Da/St$ )	0.5–1 (c)	thermal safety critical index in semi-batch reactors for fast reactions and improper heat taking-out system	
6	batch temperature (°C)	60 (d)	prevent toluene solvent excessive vaporization, pressure increase, and dangerous exothermic side-reactions	

Notes: (a) Ruppen *et al.*;<sup>2</sup> (b) Martinez;<sup>43</sup> (c)  $Da = \frac{(-v_D)r_D\tau_D}{c_{D,0}}$ ;  $St = \frac{U A_r \tau_D}{V \bar{\rho} \bar{c}_p}$ , where D = key reactant,  $(-v_D)$  = stoichiometric number of D reactant;  $\tau_D$  = time of addition of the (co-)reactant;<sup>21</sup> (d) evaluated by adding  $\Delta T_c = R T_0^2/E = 10$  K to the nominal temperature.

$B = 8.1$  (reaction #3) (i.e. larger than the threshold 5). The adiabatic induction time to explosion of  $\tau_{ad} = (k_0 B)^{-1} \approx 4$  min for reaction #3 (eq. (2)) confirms the conclusion that acetoacetylation of pyrrole and diketene oligomerization are highly dangerous reactions.

The examined SBR is the bench-scale standard jacketed reactor used by Ruppen *et al.*<sup>2</sup> for determining the kinetic data and the optimal feeding policies that maintain the reactor within safety limits and lead to an acceptable PAA yield. The characteristics of the reactor and the nominal operating conditions are taken from literature and presented in Table 2. The parameter ranges reported by various authors have been determined through experimental observations or repeated simulations of the isothermal reactor until the process constraints have been fulfilled. The threshold values used by the technological constraints of Table 2 are derived from productivity requirements (constraint no. 1), from empirical observations on safe operating

conditions (constraints no. 2, 3 and 6), or from critical engineering numbers known from literature (constraints no. 4 and 5, see also eq. (2)). It should be mentioned that a tight control of the reactor is necessary to simultaneously fulfill all such requirements, as indicated by the quite tightly allowed range of the process parameters. For instance, a rough evaluation of the critical temperature variation with the Semenov BR relationship  $\Delta T_c = (T - T_0)_c = R T_0^2 / E$ , indicates for diketene oligomerization a value of ca. 10 K (ca. 60 °C for the reacting mixture), and a critical conversion of  $X_c \approx 1/B = 0.012$  (if the overall reaction might be assumed as being of zero-order).

For the SBR, a perfectly mixed ideal model has been adopted.<sup>46</sup> The solution of the co-reactant (diketene) is continuously added with a feed flow-rate  $Q(t)$  over a pyrrole solution into the reactor, of known initial composition (including impurities coming from previous batches). The mass and heat balance equations presented in Table 3, explic-

Table 3 – Semi-batch reactor model<sup>2,46</sup>

Differential balance equations:	Observations
species mass balance: $\frac{dc_D}{dt} = (-\tilde{r}_a - 2\tilde{r}_b - \tilde{r}_c - \tilde{r}_d) + (c_{D,in} - c_D) \frac{Q(t)}{V(t)}$ $\frac{dc_P}{dt} = -\tilde{r}_a - c_P \frac{Q(t)}{V(t)}$ $\frac{dc_{PAA}}{dt} = (\tilde{r}_a - \tilde{r}_d) - c_{PAA} \frac{Q(t)}{V(t)}$ $\frac{dc_{DHA}}{dt} = \tilde{r}_b - c_{DHA} \frac{Q(t)}{V(t)}$	– At $t = 0$ ; $c_j = c_{j,0}$ ; $T = T_0$ . – reaction #3 rate is not corrected with the catalyst dilution due to other promotion mechanism – for reaction #3 the stoichiometric coefficient was included in the rate constant
volume variation: $\frac{dV}{dt} = Q(t)$	Notations: D = diketene P = pyrrole PAA = 2-acetoacetyl pyrrole DHA = dehydroacetic acid
reaction rate correction with the catalyst dilution: $\tilde{r}_j = r_j \frac{V_0}{V(t)}$ ; $j = a, b, d$	
heat balance: $\frac{dT}{dt} = \frac{Q(t)(T_{in} - T)}{V(t)} + \frac{\sum_j (-\Delta_r H)_j \tilde{r}_j V(t) - U A_r (T - T_a)}{\bar{\rho} \bar{c}_p V(t)}$ $j = a, b, c, d$	

#### Model hypotheses:

- semi-batch reactor model with perfect mixing and a uniform concentration and temperature field
- reactor of cylindrical geometry with variable liquid volume and heat transfer area:  $A_r = \frac{\pi d_r^2}{4} + \frac{4}{d_r} V(t)$
- heat transfer coefficient computed with the formula:  
 $\frac{1}{U} = \frac{1}{h_i} + \frac{\delta_i}{\lambda_i} \frac{A_r}{A_m} + \frac{1}{h_e} \frac{A_r}{A_e}$ ;  $\frac{h_i d_r}{\lambda} = 0.36 Re^{0.66} Pr^{0.33} \left( \frac{\mu}{\mu_w} \right)^{0.14}$   
 (approximate value for nominal conditions is  $U = 581.4 \text{ W m}^{-2} \text{ K}^{-1}$ )
- heat of solvent vaporisation in the reactor ( $q_{evap}$ ) is neglected
- heat capacity and density of feeding solution are the same with those of reactor content,  $\bar{\rho}_{in} \bar{c}_{p,in} = \bar{\rho} \bar{c}_p$

$$- Re = \left( \frac{d_r^2 n \bar{\rho}}{\mu} \right)$$

$$- Pr = \left( \frac{\bar{c}_p \bar{\mu}}{\lambda} \right)$$

itly account for the liquid volume variation due to the added diketene solution. The volume increase is considered when up-dating the heat transfer area of the jacketed reactor, while the continuous catalyst dilution is accounted when correcting the reaction rates. This assumption, however, does not apply for reaction #3 because the diketene oligomerization is presumed to be promoted not by pyridine but by other intermediate products (of a quasi-constant total concentration). To speed-up the computational steps, the physical properties of the reaction mixture have been approximated to those of the toluene solvent, and a constant overall heat transfer coefficient has been adopted (evaluated at nominal conditions with the formula of Table 3). The reactor model has been solved with a common low order stiff differential equation integrator.

### Reactor thermal sensitivity and critical operating conditions

Due to the reactor operating constraints imposed by a pre-established productivity and safety requirements, a tight control of the temperature and an optimal feeding policy with diketene are necessary. Several studies have been published that solve this optimal control problem, by applying various numerical procedures that find the optimal molar feed flow-rate of diketene ( $Qc_{D,in}$ )( $t$ ) under isothermal conditions which, for a constant concentration  $c_{D,in}$ , corresponds to finding the optimal feed flow-rate  $Q(t)$ . The results have been obtained by solving the nonlinear programming problem (NLP) associated with finding the optimum value of a performance criterion, such as:

- minimization of the (semi-)batch reactor operating time ( $t_f$ ) under the constraints #1–3 (Table 2), and using various approaches: i) without including<sup>47</sup> or, ii) with including rate constant up-dating steps by using on-line measured data;<sup>2,19,48</sup> iii) by considering a certain number (e.g. eight) of step-variations of the feed flow rate, the dynamic model being collocated on equally distributed super-elements, and approximating the state variable evolution with quadratic polynomials;<sup>49</sup>

- maximization of the PAA yield (for a fixed  $t_f$ ) under the constraint  $c_{DHA}(t_f) + c_F(t_f) < c_{max}$ , by using a penalty barrier function added to the cost in order to penalize the production of the undesired species DHA and F;<sup>50</sup>

- determine the optimal  $t_f$  that maximize the PAA yield under the constraint #2–3 (Table 2), by using a variant of the Simplex algorithm.<sup>43</sup>

Solutions of these optimization trials suffer from two major drawbacks: they do not consider the temperature dynamics during the batch (i.e. the

energy differential balance of the reactor) and, they do not consider a preliminary risk assessment step when specifying the runaway boundaries in the parametric space (i.e. safety operating region). Simple setting of safety constraints by means of semi-empirical observations, or a rough evaluation using approximate explicit criteria (such as  $\Delta T_c = RT_0^2/E$ , and  $X_c \approx 1/B$ ) are not enough to correctly set the search region in the parameter space.

To solve the risk assessment problem, one uses a step-by-step approach in order to determine the critical operating limits. The first step is to perform a local sensitivity analysis of the reactor by successively perturbing the main operating parameters around the nominal point to roughly: i) establish the most influential variables of the process, and ii) to guess the critical region of high thermal sensitivity in the parameter space.

To precisely determine the critical operating conditions of the SBR with the MV method, it is necessary to investigate the regions for which the state variables (and especially the reactor temperature) exhibit high sensitivities to the operating conditions, even if such set points will not be later used as nominal operating values. Thus, moving the set point in a more sensitive region and performing repeated simulations of the reactor dynamics, the precision in determining the critical conditions is considerably improved.<sup>23</sup>

By simulating the semi-batch reactor behaviour at various constant feed flow rates  $Q$  (of a constant  $c_{D,in}$  concentration), the dynamics of the temperature, species concentrations, P-conversion and PAA-yield, reaction rates, reaction Damköhler ( $Da$ ) or Damköhler/Stanton ( $Da/St$ ) numbers are obtained and plotted in Fig. 1 (keeping all other parameters at nominal values). It should be noted that, starting with  $Q = 0.0083 \text{ L min}^{-1}$ , the temperature  $T(t)$  profile not only exhibits values higher than 60 °C, but the curve tends to oscillate. An increase in the feed flow rate to  $Q = 0.0090 \text{ L min}^{-1}$  produces large amplifications of oscillations leading to reactor runaway. Due to secondary reactions, for feeding rates of D solution higher than a critical value, the reactor temperature reaches levels higher than the adiabatic rise corresponding to the main reaction #1, that is  $T_0 + \Delta T_{ad,1} = 50 + 61.8 = 111.8 \text{ °C}$ .

Such an effect can be explained by the slow secondary reactions #2–3 which become dangerous when the co-reactant D is accumulating at low temperatures (for  $Da < 50$  and  $Da/St < 1$  numbers in Fig. 1). When the  $Q$ -level is small, the main reaction consumes the co-reactant, the side-reactions are negligible, and the temperature time-profile is quite flat. For high  $Q$ -levels, the slow side-reactions

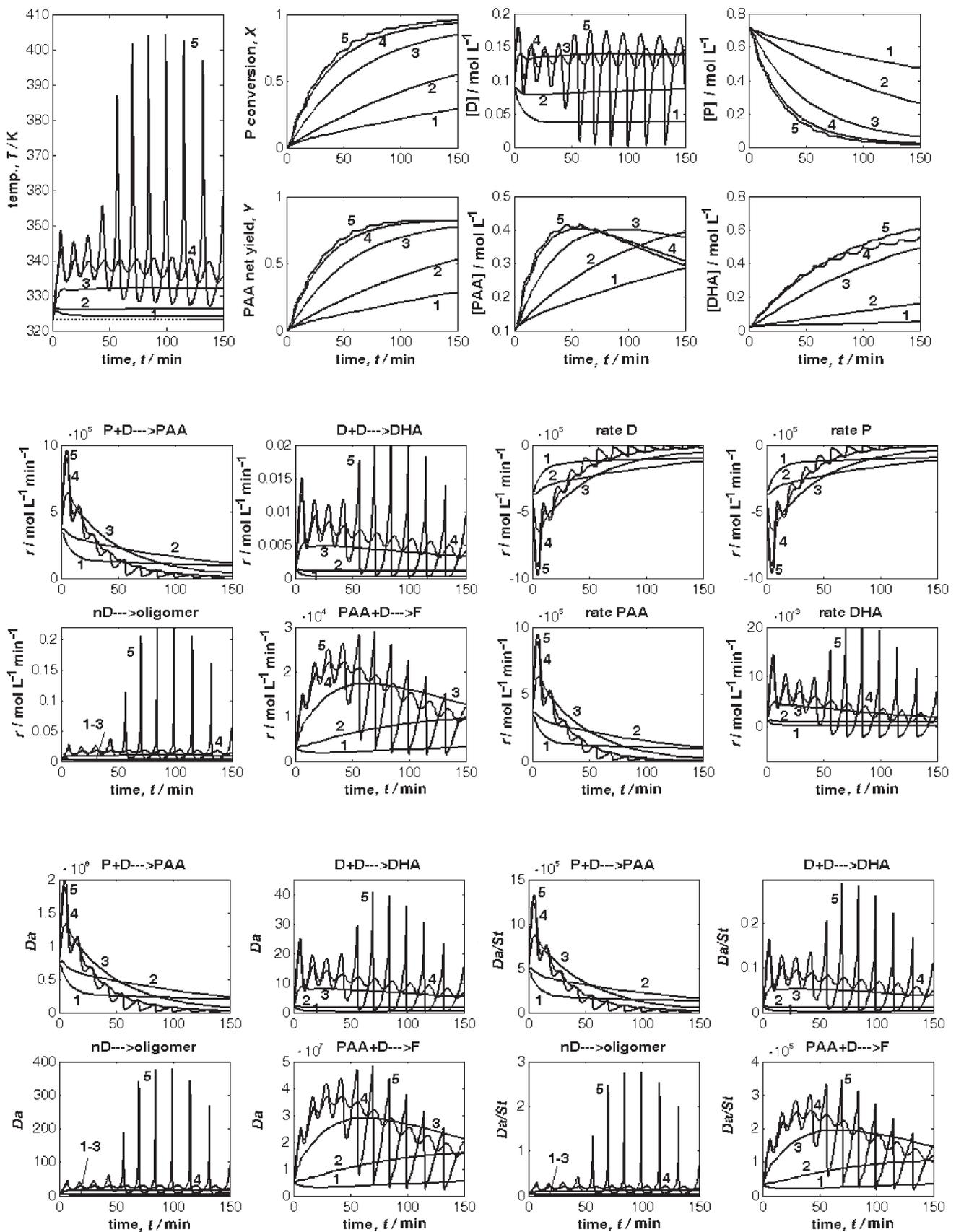


Fig. 1 – Dynamics of the reactor state-variables (temperature and concentrations), reaction rates (#1–4), species transformation rates ( $\tilde{r}_i$ ), Damköhler number ( $Da$ ), and  $Da/St$  number ( $St = Stanton$ ). The curve indices correspond to constant  $Q = 0.0005 \text{ L min}^{-1}$  (1);  $Q = 0.0015 \text{ L min}^{-1}$  (2);  $Q = 0.0050 \text{ L min}^{-1}$  (3);  $Q = 0.0083 \text{ L min}^{-1}$  (4);  $Q = 0.0090 \text{ L min}^{-1}$  (5), under constant nominal conditions ( $T_a = T_0 = T_m = 323 \text{ K}$ , see Table 2).

of constants  $\tau = 1/k_0$  smaller than the co-reactant adding time  $\tau_D$ , lead to the co-reactant D accumulation. Consequently, the increased rates of side reactions will start to generate more energy that will increase the reactor temperature. In turn, a high temperature will lead to the increase of all reaction rates (Fig. 1), and to a rapid consumption of the D co-reactant. Quick depletion of D will slow down the reaction rates, and consequently diminish the generated heat, thus decreasing the reactor temperature. At low temperatures, the accumulation of the co-reactant is again possible due to the reduced reaction rates, and a new temperature cycle starts again. The result is a continuous oscillation of the reaction temperature, with amplitudes as large as the  $Q$ -level is higher. When exceeding a certain critical  $Q_c$  value, the reactor oscillations are amplified, leading to escalation of the side reactions and explosion, since the cooling system cannot remove the heat at the same rate. In the present case, the nominal operation at  $Q = 0.0015 \text{ L min}^{-1}$  ensures a 53.1 % PAA net yield and fulfillment of constraint #2 (Table 2). The final  $c_D(t_f) = 0.08 \text{ mol L}^{-1}$  may require a slight decrease in  $Q$  in the range of  $0.0010\text{--}0.0015 \text{ L min}^{-1}$ , with a predicted thermal peak of 2–3 K.

To study the influence of the cooling agent temperature ( $T_a$ ) on the reactor dynamics, the simulated results for  $T_a = 20 \text{ }^\circ\text{C}$  using the same range of feed flow-rates  $Q \in [0.0005\text{--}0.0090] \text{ L min}^{-1}$  are displayed in Fig. 2. The time-plots reveal a strong influence of  $T_a$ . Small reactor temperatures lead to smaller PAA yields even for flow-rates higher than  $Q_c = 0.0083 \text{ L min}^{-1}$ . Consequently, evaluation of  $Q_c$  runaway boundary requires taking into account the influences of all operating parameters.

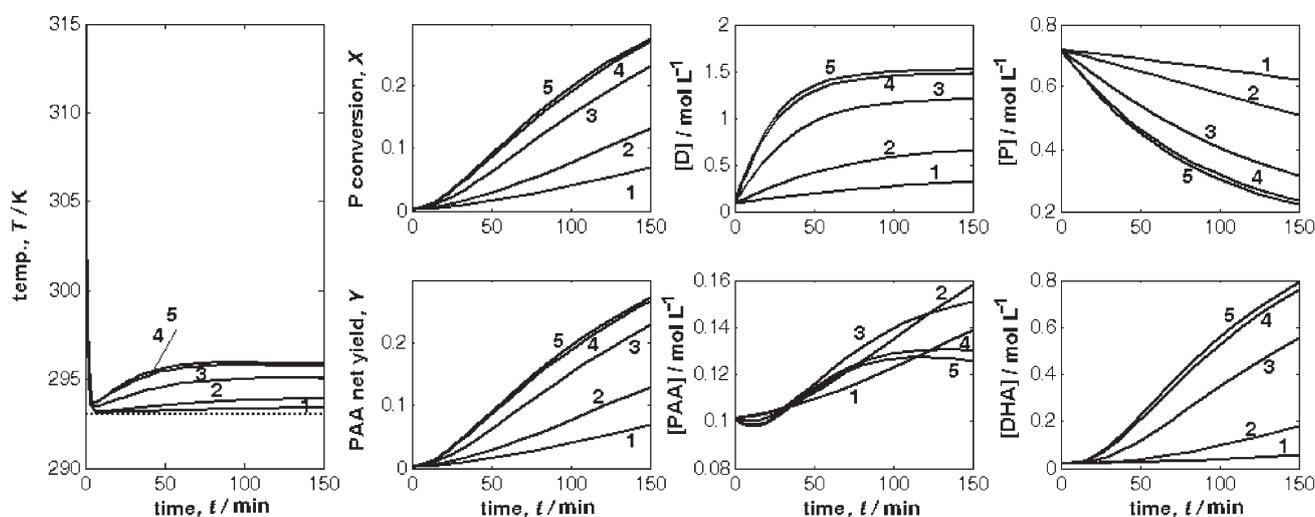


Fig. 2 – Dynamics of the reactor state-variables (temperature, concentrations, P-conversion, PAA-yield) for a cooling agent of temperature  $T_a = 293 \text{ K}$ . The curve indices correspond to constant  $Q = 0.0005 \text{ L min}^{-1}$  (1);  $Q = 0.0015 \text{ L min}^{-1}$  (2);  $Q = 0.0050 \text{ L min}^{-1}$  (3);  $Q = 0.0083 \text{ L min}^{-1}$  (4);  $Q = 0.0090 \text{ L min}^{-1}$  (5), under constant nominal conditions (Table 2).

Various reactor dynamics scenarios can be simulated by consecutively modifying individual operating variables from their nominal values. The obtained state-variable time-profiles for various  $c_{D,in} \in [4\text{--}6] \text{ mol L}^{-1}$  are plotted in Fig. 3, and the reactor dynamics for various  $c_{P,0} \in [0.4\text{--}0.8] \text{ mol L}^{-1}$  in Fig. 4. Thus, one can conclude that the most influential variables for the process safety are  $Q$ ,  $T_a$ ,  $c_{D,in}$ , and  $c_{P,0}$ . The batch initial temperature presents a small influence on the reactor dynamics (plots not presented here), while small variations of the initial concentrations for other species than pyrrole does not present high interest as long as the composition is roughly constant and determined by the reactant P recovering system.

In a second step, a systematic determination of the runaway boundaries for the main operating parameters  $\phi = [Q, T, c_{D,in}, c_{P,0}]$  can be done by several methods. For instance, a geometry-based method will determine the critical runaway conditions from the temperature – time plot  $T(t)$  in Fig. 1, corresponding to the first recorded inflexion point before the curve first maximum. A more precise way is to apply the generalized MV sensitivity criterion. In the present study, the numerical evaluation of sensitivities  $s(T; \phi)$  with finite differences has been applied, by replacing the derivatives with  $s(y; \phi_j)_t = \Delta y(t) / \Delta \phi_j$ . The time discretization step has been set to  $t_f/5000$  in order to consider all temperature peaks in the critical operating region. The size of the discretization step in evaluating the sensitivity functions has been set to ensure a satisfactory precision, at a level of  $(\phi_{\max} - \phi_{\min})/n$ , with  $n = 200\text{--}500$ .

Application of the MV criterion starts with evaluating the runaway boundaries in the  $Q\text{--}T_a$

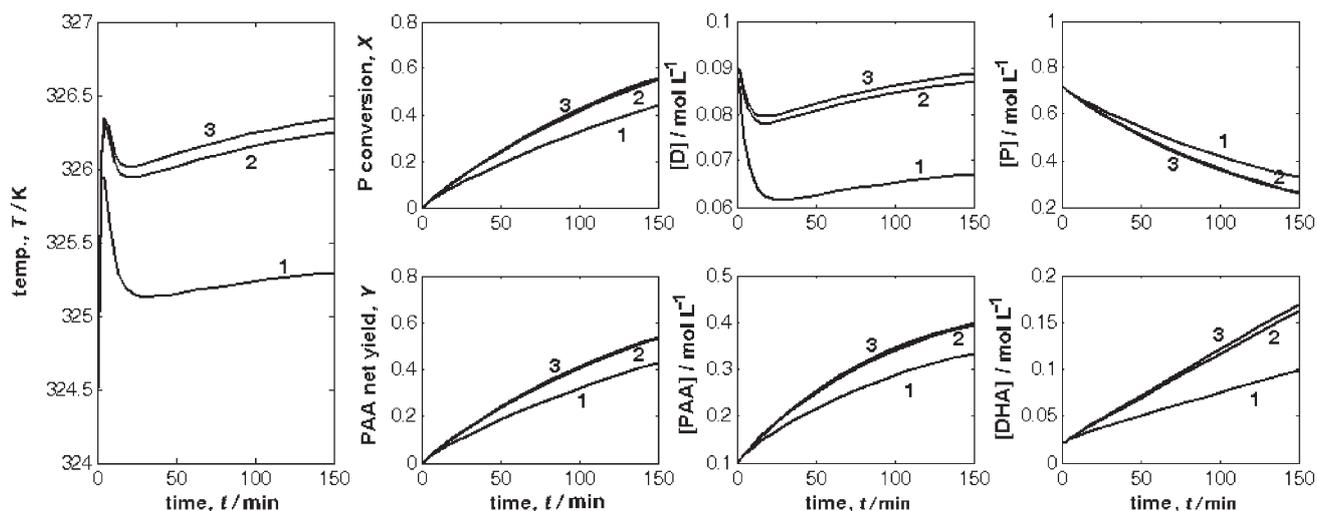


Fig. 3 – Dynamics of the reactor state-variables (temperature, concentrations, P-conversion, PAA-yield) for several inlet D concentrations  $c_{D,in}$  of 4 mol L<sup>-1</sup> (1), 5.82 mol L<sup>-1</sup> (2), and 6 mol L<sup>-1</sup> (3), under constant nominal conditions (Table 2)

plane, by keeping nominal states for all other parameters. Repeated simulations of the semi-batch reactor dynamics for various  $Q$ -levels and a certain  $T_a$ , lead to the evaluation of  $s(T; Q)_t$  time-profile, and determination of the sensitivity of the maximum temperature in the reactor in absolute  $s(T_{max}; Q)$  or relative  $S(T_{max}; Q)$  terms. By plotting the resulted  $S(T_{max}; Q)$  values for every checked  $Q$ -level, the curves of Fig. 5 (left) are obtained. The computational cycle is repeated, every displayed curve in Fig. 5 corresponding to a certain cooling temperature  $T_a$ . It should be noted that, for every  $T_a$ , a sharp increase in the  $S(T_{max}; Q)$  is recorded for  $Q > Q_c$ . The critical values  $Q_c$  determined in this way are then represented in the  $Q - T_a$  plane, and the runaway critical curve  $Q_c(T_a)$  is thus obtained. The runaway boundary (the solid curve in Fig. 5 – right) divides the  $Q - T_a$  plane into two regions, corre-

sponding to a safe or an unsafe operation of the reactor. As expected, the critical feed flow rate  $Q_c$  decreases as the operating severity increases, that is for high  $T_a$  temperatures.

Similar application of the MV generalized criterion results in calculation of the runaway boundary in the  $Q - c_{D,in}$  plane (Fig. 6), and in the  $Q - c_{P,0}$  plane (Fig. 7). It should be noted that the inlet concentration of the D co-reactant exerts a strong influence on the critical  $Q_c$  values, leading to a decrease of  $Q_c$  for higher  $c_{D,in}$ . In fact, the critical inlet parameter is not the solution flow-rate  $Q_c$ , but the molar feeding rate with D co-reactant, that is the product ( $Qc_{D,in}$ ). Keeping in mind that all calculations for critical  $Q_c$  have been done for a constant  $c_{D,in} = 5.82$  mol L<sup>-1</sup> (nominal value), extension of the validity of the runaway boundary plots of Figs. 5–7 can be easily performed by replacing

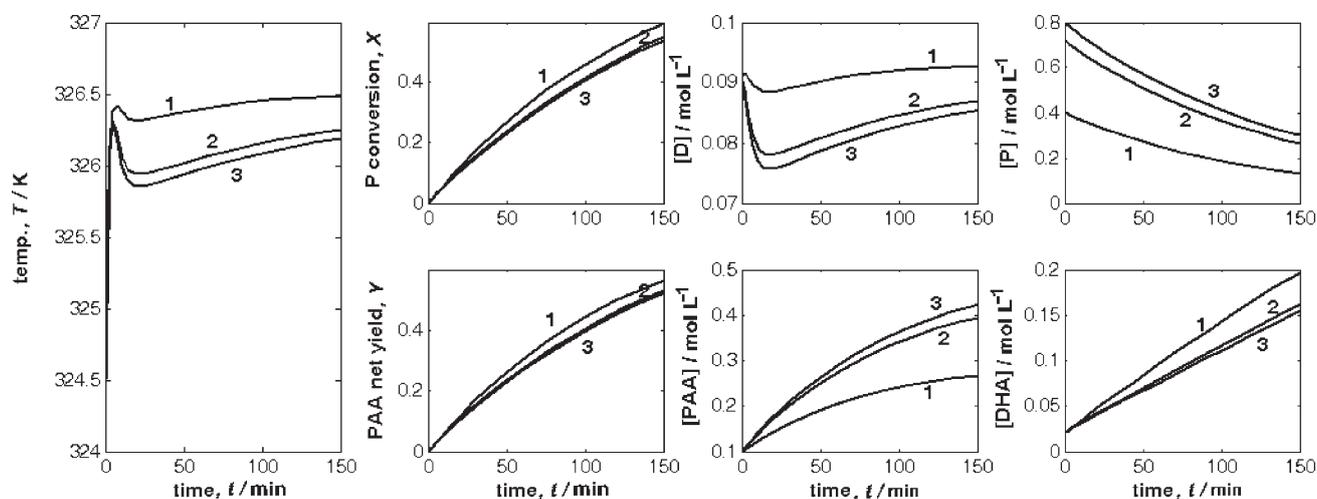


Fig. 4 – Dynamics of the reactor state-variables (temperature, concentrations, P-conversion, PAA-yield) for several initial P concentrations  $c_{P,0}$  of 0.4 mol L<sup>-1</sup> (1), 0.72 mol L<sup>-1</sup> (2), and 0.8 mol L<sup>-1</sup> (3), under constant nominal conditions (Table 2)

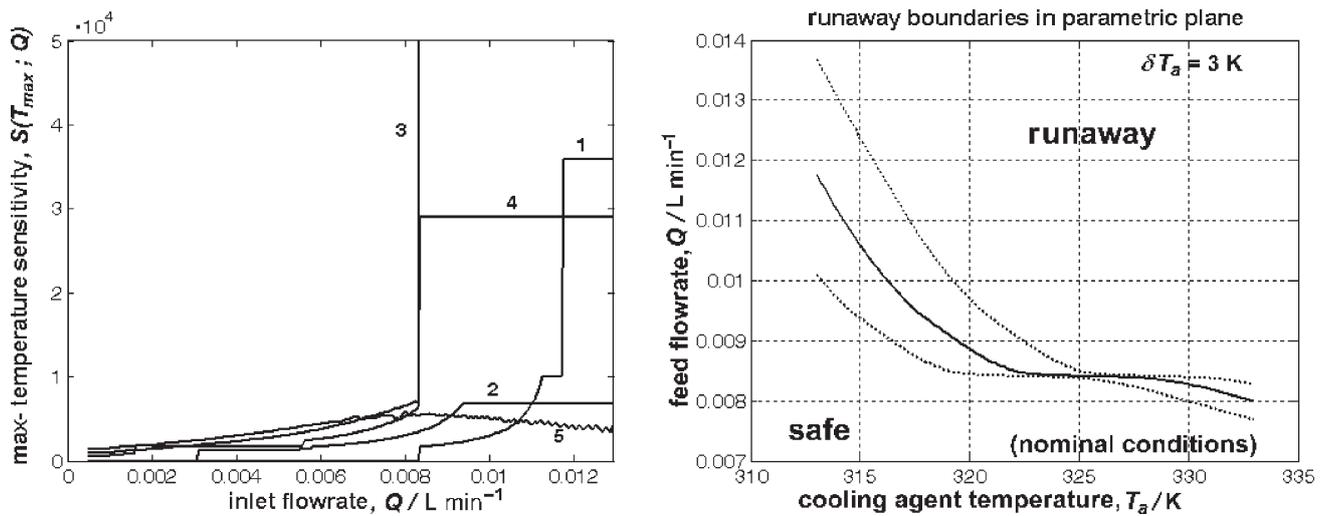


Fig. 5 – (Left) Sensitivity of the reactor maximum temperature to the feed flow rate for various cooling agent temperatures of 313 K (1), 318 K (2), 323 K (3), 328 K (4), and 333 K (5), under constant nominal conditions. (Right) Runaway boundaries in the  $[F \text{ vs. } T_a]$  plane at nominal conditions. The confidence band (---) corresponds to the random deviations in the range of  $\delta T_a = \pm 3 \text{ K}$ .

the  $Q_c$  in the ordinate with the product ( $5.82 Q_c$ ) mol D  $\text{min}^{-1}$ . Thus, the estimated boundary curve diagrams in the operating parameter planes can be used for checking operation at various feeding solution concentrations.

The same procedure can be applied by considering every other parameter. The temperature sensitivity vs. the operating parameter  $\phi_j$  can be obtained simply by replacing the corresponding terms in the sensitivity equation and by plotting the resulted  $s(T_{max}; \phi_j)$  for various  $\phi_j$  values. Bringing together all these runaway limit curves in various parameter planes it is possible to obtain the global sensitivity of the reactor by accounting for concomitant variations in several input/process parameters. Also, it

should be mentioned that evaluated  $s(T; Q_{in})$  and  $s(T; T_0)$  correspond in fact to Green's functions (eq. (6)).

Based on the obtained critical values  $Q_c$  evaluated with the MV-criterion (Figs. 5–7), it is possible to empirically correlate them with the operating parameters. Because of the process nonlinearity, a nonlinear empirical model should be employed in this respect. Indeed, a logarithmic type algebraic model has been found to adequately represent the critical reactor conditions vs. the main operating parameters for this type of catalyst:

$$\ln(\tilde{Q}_c) = 26.6766425 - 5.1050358 \ln(T_a) - 1.05356372 \ln(c_{D,in}) + 0.186367982 \ln(c_{P,0}). \quad (7)$$

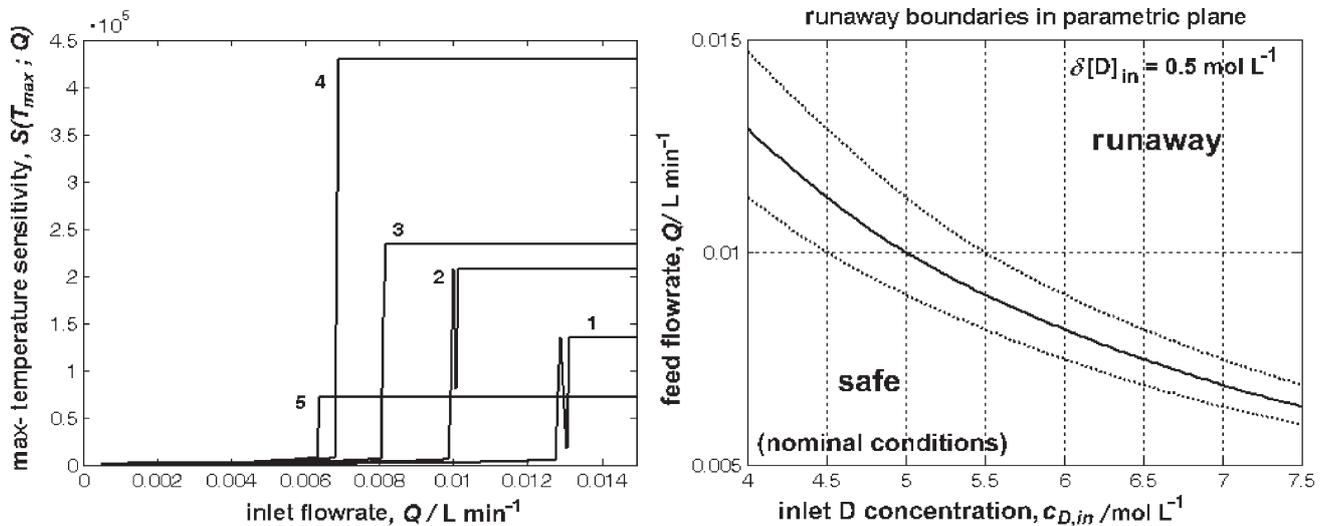


Fig. 6 – (Left) Sensitivity of the reactor maximum temperature to the feed flow rate for various inlet D concentrations of 4 mol  $L^{-1}$  (1), 5 mol  $L^{-1}$  (2), 6 mol  $L^{-1}$  (3), and 7 mol  $L^{-1}$  (4), under constant nominal conditions. (Right) Runaway boundaries in the  $[Q \text{ vs. } c_{D,in}]$  at nominal conditions. The confidence band (---) corresponds to the random deviations in the range of  $\delta c_{D,in} = \pm 0.5 \text{ mol } L^{-1}$ .

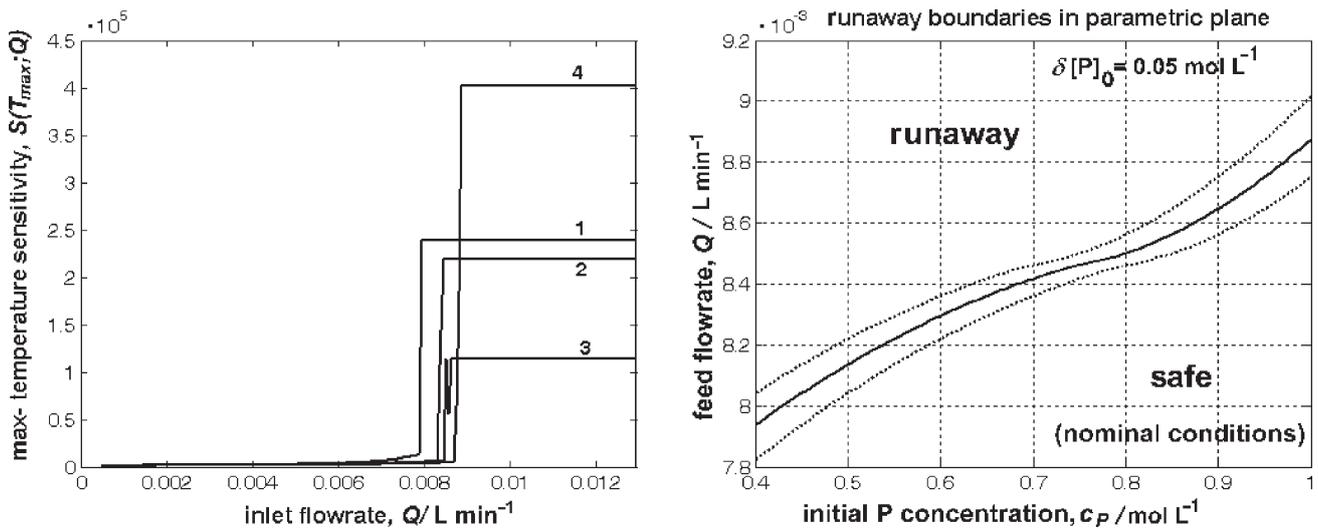


Fig. 7 – (Left) Sensitivity of the reactor maximum temperature to the feed flow rate for various initial P concentrations of 0.4 mol L<sup>-1</sup> (1), 0.72 mol L<sup>-1</sup> (2), 0.80 mol L<sup>-1</sup> (3), and 1.00 mol L<sup>-1</sup> (4), under constant nominal conditions. (Right) Runaway boundaries in the  $[Q \text{ vs. } c_P]$  at nominal conditions. The confidence band (---) corresponds to the random deviations in the range of  $\delta c_{P0} = \pm 0.05 \text{ mol L}^{-1}$ .

The model prediction standard deviation is satisfactorily low ( $8.9 \cdot 10^{-5} \text{ L min}^{-1}$  for the predicted  $Q_c$ ), and as the relative residuals (avg. 4.4 %), the residuals being alternatively positive and negative (see Maria<sup>51</sup> for more complete model adequacy and parameter inference tests).

Parameter uncertainty, due to random variations of type  $\bar{\phi}_j \pm \delta\phi_j$ , can be accounted for when deriving the safety limits by evaluating the associated confidence region with the MV-sensitivity method, alternatively considering the parameters at lower or upper bounds. Thus, the lower and upper bounds of the critical conditions can be obtained, while the confidence band in the parametric plane corresponds to a 100 % confidence level if parameters are uniformly distributed, or to a lower confidence level for normal distributed parameters depending on the distribution characteristics (i.e. a 68 % confidence level for  $\delta\phi_j = \sigma_{\phi_j}$ , a 95 % confidence level for  $\delta\phi_j = 2\sigma_{\phi_j}$ , etc., where  $\sigma$  denotes the standard deviation). For instance, the resulted confidence bands for  $\delta T_a = 3 \text{ K}$ ,  $\delta c_{D_{in}} = 0.5 \text{ mol L}^{-1}$ ,  $\delta c_{P,0} = 0.05 \text{ mol L}^{-1}$  are presented in Figs. 5–7 (with dotted lines). Based on the statistical model (7), the approximate variance of  $Q_c$  can then be evaluated by using the well-known error propagation formula.<sup>56</sup>

Such an uncertainty in the operating parameters must be considered when determining the optimal operating policy of the SBR, usually by taking the maximum sensitivities as constraints, and keeping the solution inside the random variation region that never intersects the constraints boundaries or, for a certain confidence level, without intersecting the confidence band itself.

Finally, it is worth noting that a preliminary investigation of the thermal and kinetic sensitive region location in the parametric space is necessary (by means of the process model), followed by a re-location of the set point in such a region for increasing the precision in determining the critical SBR conditions. Based on precise results, a simple correlation of the critical conditions with the operating parameters can be obtained, to be further used together with the computed sensitivities of the state variables, as constraints when deriving the optimal operating conditions of the SBR by means of a certain optimization criterion.<sup>11,15</sup>

Generally, for a complex kinetics, comprising a large number of species and reactions, application of the MV runaway criterion in order to determine the runaway boundaries, for all influential parameters and initial/inlet conditions of the reactor, is a fairly computational task. However, if enough information is available, the runaway conditions can be predicted accurately. To save time, it is preferable to reduce the number of the considered key reaction steps, for instance, by applying the rate-limiting step theory, the sensitivity analysis, or another systematic rule for kinetic model reduction (reviews of Maria<sup>51,52</sup>).

## Conclusions

Periodic determination of the safe operating limits for a SBR exhibiting a high thermal sensitivity, especially when the catalyst or raw-material characteristics fluctuate, is an engineering problem of current interest. The safety problem is also related to the economic implications of getting a

higher productivity by setting the nominal operating point in a vicinity of the safety limits.

A quick assessment of the runaway conditions, by means of shortcut methods using engineering numbers and simple overall kinetic models, can offer a rough picture on the safety limits, without involving a reactor model. The disadvantage consists in setting of too conservative margins of safety, usually corresponding to milder operating conditions leading to unfavourable economic effects.

When more information about the process and catalyst characteristics is available, sophisticated but more precise safety analyses can be applied. By using a relatively simple reactor model, the application of a local and global sensitivity analysis or a generalized sensitivity criterion leads to an accurate estimation of the safety margins of the operating region and helps setting the nominal point at an economically favourable location.

In spite of being more computational than other sensitivity criteria, the MV generalized sensitivity criterion can offer a satisfactory prediction of the runaway conditions for the semi-batch reactor, being generally applicable both to simple or complex reactor/process models.

For the example presented in this paper, the reactor performance can be conveniently enhanced by adjusting the feeding policy of diketene ( $Q_{C_{D,in}}(t)$ ), or by choosing a time-dependent cooling agent temperature  $T_a(t)$  policy. In both alternatives, optimization of a performance criterion has to be related to the runaway boundaries accurately determined by means of the MV criterion. Operating conditions located at a certain distance from the runaway boundaries is expected to lead to better policies for reactor feeding and temperature (leading to higher PAA yields) than those derived by simply restrict the search region based on semi-empirical safety constraints.

The study also points-out that parameter random fluctuations have to be considered not only in determining the new operation set point of the reactor, but also when evaluating the confidence of safety region according to the parameter distribution. Optimal solutions kept inside the random variation region, without intersecting the confidence band of the runaway boundaries, are expected to offer a higher degree of safety in operation with the expense of a certain decline in reactor productivity.

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#### Notations

- $A_r, A_e, A_m$  – heat exchange surface of the reactor:  $A_r$  is measured inside the reactor;  $A_e$  is measured cooling fluid side;  $A_m$  is the logarithmic mean between  $A_r$  and  $A_e$ ,  $m^2$
- $A$  – Arrhenius frequency factor,  $L \text{ mol}^{-1} \text{ s}^{-1}$ ,  $s^{-1}$
- $ADT_{24}$  – sample initial temperature for an adiabatic decomposition within  $TMR_{ad} = 24$  hours, K
- $B = \Delta T_{ad} E / (RT_0^2)$  – reaction violence index<sup>21</sup>
- $c_j$  – component  $j$  concentration,  $\text{mol L}^{-1}$
- $c_p$  – specific heat capacity,  $\text{J kg}^{-1} \text{ K}^{-1}$
- $d_r$  – reactor inner diameter, m
- $d_s$  – stirrer diameter, m
- $Da = (-v_A)(r_A \tau_D) / c_{A,0}$  – Damköhler number for SBR
- $E$  – activation energy,  $\text{J mol}^{-1}$
- $Q$  – feed flow rate (liquid),  $\text{L s}^{-1}$
- $\mathbf{g}$  – model function vector
- $\mathbf{G}$  – Greens’ function matrix
- $H_f^\circ$  – standard enthalpy of species formation,  $\text{J mol}^{-1}$
- $(-\Delta_r H)$  – reaction enthalpy,  $\text{J mol}^{-1}$
- $h_e$  – reactor convective heat transfer coefficient, on the cooling agent side,  $\text{W m}^{-2} \text{ K}^{-1}$
- $h_i$  – heat transfer coefficient, on the reactor side,  $\text{W m}^{-2} \text{ K}^{-1}$
- $I_{h_i}$  – the increments of structural groups  $i$  for enthalpy of formation in the Joback formula,<sup>53</sup>  $\text{kJ mol}^{-1}$
- $\mathbf{J} = \partial \mathbf{g} / \partial \mathbf{x}$  – system Jacobian
- $k$  – rate constants,  $\text{L mol}^{-1} \text{ s}^{-1}$ ,  $\text{s}^{-1}$
- $n_j$  – amount of species  $j$ , mol
- $n$  – reaction order or, number of discretization steps or, stirrer speed,  $\text{s}^{-1}$
- $Pr$  – Prandtl number
- $p$  – overall pressure, Pa
- $q_G, q_T$  – generated and released heat fluxes,  $\text{W m}^{-2}$
- $R$  – universal gas constant,  $\text{J mol}^{-1} \text{ K}^{-1}$
- $Re$  – Reynolds number
- $r$  – chemical reaction rate,  $\text{mol L}^{-1} \text{ s}^{-1}$
- $s_i$  – the number of structural groups of type  $i$  (in the chemical formula)
- $s(y; \phi)$  – absolute sensitivity,  $\partial y(z) / \partial \phi$
- $S(y; \phi)$  – normalized sensitivity,  $(\phi^* / y^*) s(y; \phi)$
- $St = (U A_r \tau_D) / (V \bar{\rho} \bar{c}_p)$  – Stanton number for SBR
- $t$  – time, s
- $T$  – temperature, K
- $T_{onset}$  – temperature of the first step change in the recorded heat flux thermograms with the dual scanning calorimetry, K
- $\Delta T_{ad}$  – temperature rise under adiabatic conditions, K

$TMR_{ad}$  – time-to-maximum-rate under adiabatic conditions, s  
 $U$  – overall heat transfer coefficient,  $W\ m^{-2}\ K^{-1}$   
 $V$  – liquid (reactor) volume,  $m^3$   
 $x$  – state variable vector  
 $X_j$  – reactant  $j$  conversion  
 $y$  – state variable vector  
 $Y$  – yield

### Greeks

$\Delta$  – finite difference  
 $\delta$  – Kronecker delta function  
 $\delta_t$  – reactor wall thickness, m  
 $\phi$  – operating parameter  
 $\lambda_p, \lambda$  – thermal conductivity of the reactor material; thermal conductivity,  $W\ m^{-1}\ K^{-1}$   
 $\lambda_j$  – eigenvalues of a matrix  
 $\mu$  – dynamic viscosity, Pa s  
 $\nu_j$  – stoichiometric number of species  $j$   
 $\rho$  – liquid phase density,  $kg\ m^{-3}$   
 $\sigma$  – standard deviation  
 $\tau$  – time constant, s  
 $\tau_{ad}$  – induction time to explosion under adiabatic conditions, s  
 $\tau_D$  – time of addition of co-reactant D, s  
 $\varphi$  – volume fraction, %

### Index

a – cooling agent  
 ad – adiabatic  
 c – critical  
 f – final  
 in – inlet  
 l – liquid phase  
 max – maximum  
 min – minimum  
 0 – initial  
 w – wall

### Abbreviations

CPQRA – chemical process quantitative risk analysis  
 D – diketene  
 DHA – dehydroacetic acid  
 EAL – equipment risk assessment level  
 FDM – finite difference method  
 MV – Morbidelli-Varma criterion

P – pyrrole  
 PAA – 2-acetoacetyl pyrrole  
 RAL – reactivity assessment level  
 SAL – substance risk assessment level  
 STAL – safety-technology assessment level

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