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Towards the Grand Unification of Process Design, Scheduling, and Control—Utopia or Reality?

Baris Burnak [1,2], Nikolaos A. Diangelakis [1,2] and Efstratios N. Pistikopoulos [1,2,*]

[1] Artie McFerrin Department of Chemical Engineering, Texas A&M University, College Station, TX 77845, USA
[2] Texas A&M Energy Institute, Texas A&M University, College Station, TX 77845, USA
* Correspondence: stratos@tamu.edu

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Abstract: As a founder of the Process Systems Engineering (PSE) discipline, Professor Roger W.H. Sargent had set ambitious goals for a systematic new generation of a process design paradigm based on optimization techniques with the consideration of future uncertainties and operational decisions. In this paper, we present a historical perspective on the milestones in model-based design optimization techniques and the developed tools to solve the resulting complex problems. We examine the progress spanning more than five decades, from the early flexibility analysis and optimal process design under uncertainty to more recent developments on the simultaneous consideration of process design, scheduling, and control. This formidable target towards the grand unification poses unique challenges due to multiple time scales and conflicting objectives. Here, we review the recent progress and propose future research directions.

Keywords: process design; scheduling; process control; integration

1. Introduction

It has been over half a century since Professor Roger W.H. Sargent envisioned a paradigm shift in chemical process design methodologies, from ad hoc engineering judgment for specific problems to fully computerized systematic approaches based on complex mathematical models [1]. He conceived the notions of "explicitly formulating the techniques" and "precisely defining the objectives" for engineering design problems, which used to be considered to be "an activity not worthy of higher minds" because of the lack of scientific and systematic tools and methodologies. With the advent of computers, he further emphasized the opportunity to expand the process design problem to account for foreseeable variations in the plant environment over its life cycle to achieve more reliable and robust operations. "(During the process design phase) Many parameters are left available for adjustment during plant operation, such as flow rates, tank levels, operating pressures, etc., but here also *the design places limits on the range of variation possible*." stated Professor Sargent to underpin the interdependence between the design and the uncertainty of future operational decisions.

The Process Systems Engineering (PSE) community has been accumulating formidable knowledge and know-how on mathematical modeling techniques in the fields of process design and operations, and developed efficient tools to solve these advanced models since Professor Sargent had outlined the future of PSE in his 1967 perspective article [1]. Moreover, it has been long established that the early design problem should be studied simultaneously with the operational time-variant decisions to improve the operability and flexibility of the process under variable internal and external plant conditions, and consequently to achieve more reliable, economically more favorable, and inherently safer processes. The most recent efforts towards simultaneous consideration of design and operational decisions explore effective methodologies to integrate the short-term process regulatory decisions (process control) and longer-term economical decisions (scheduling) through mixed-integer dynamic optimization (MIDO) formulations. The proposed solution tools and techniques for this class of integrated problems include (i) discretizing the dynamic high-fidelity representation of the process through orthogonal collocation on finite elements followed by solving a mixed-integer nonlinear programming problem [2], (ii) "back-off" approach to ensure constraint satisfaction under some assumed worst-case scenario [3–5], and (iii) multiparametric programming to explicitly represent the operational strategies to derive tractable and equivalent MIDO formulations [6].

In this paper, we present a historical perspective on the development and progress of modern process design techniques that account for the dynamic variability introduced by the process control and scheduling decisions. In retrospect, we observe the evolution of methodologies from fundamental analyses on design and process uncertainty at steady state to dynamic complex models that explicitly encapsulate the scheduling and control decisions, as illustrated in Figure 1, and summarized as follows.

i *Flexibility analysis and flexibility index*. The early stages for design optimization under uncertainty. The studies here analyze the steady-state feasibility of a nominal process design under a set of unknown process parameters and unrealized operating decisions, as we will discuss in Section 2.
ii *Dynamic resilience and controllability analysis*. Here, the researchers investigate the dynamic response of a system in closed loop, its interdependence with process design, and attempt to develop the "perfect controller" simultaneously the process that the controller can act on. Such attempts will be demonstrated in Section 3.
iii *Complete integration of design, control, and operational policies*. The focus of the most recent studies in the field. The goal is to model tractable dynamic design optimization problems that account for the scheduling and control decisions to guarantee the operability and even profitability of the operation under all foreseeable conditions. These approaches will be discussed in Section 4.

Clearly, it would be inaccurate and redundant trying to reduce the individual research efforts to a single category. The literature is noticeably diverse in this field with numerous different approaches. However, we find it useful to classify into certain schools of thought that are also in alignment with the historical progress of the field. In Section 5, we further seek to pose the pivotal questions on future challenges and opportunities for the seamless integration of the design, scheduling, and control problems based on the cumulative knowledge of the PSE community and the current trends in the academia.

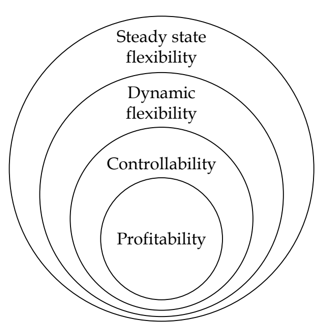

Figure 1. A Venn diagram representation of major operability indices and their relationship with process economics. It is interesting to note that the design optimization approaches started from the outermost layer, and with the advance of modeling techniques, they have progressed towards the center for guaranteed operability, which delivers the optimal process economics.

2. Early Efforts in Design Optimization under Uncertainty

The ongoing collective efforts towards the grand unification of design, scheduling, and control was inaugurated through steady-state design under uncertainty in plant conditions. Takamatsu et al. (1970) [7] estimated the undesirable effects of variations in system parameters, measured process disturbances, and manipulated variables on plant performance by sensitivity analysis on a linearized model. Nishida et al. (1974) [8] adopted the notion of sensitivity analysis to structure a min-max problem for design optimization, presented by Equation (1).

$$\begin{aligned} \min_{des} \max_{\theta} \quad & C(x, des, \theta) \\ s.t. \quad & h(x, des, \theta) = 0 \\ & g(x, des, \theta) \leq 0 \\ & \underline{\theta} \leq \theta \leq \overline{\theta} \end{aligned} \tag{1}$$

where x is the vector of states of the system, des is the vector of design variables including the steady-state manipulated variables, θ is the vector of parameters that agglomerates the system uncertainties and process disturbances. Equation (1) is one of the first notable attempts to systematically assess the trade-off between minimizing the investment cost and improving the flexibility of the process design. However, this strategy yields conservative solutions since it does not distinguish the time-invariant design variables and time-variant manipulated variables. Grossmann and Sargent (1978) [9] remedied this issue by treating the time-sensitive variables (i.e., manipulated actions and design variables that can be modified in the future) and fixed design variables separately. They further adopted the parametric optimal design problem proposed by Kwak and Haug (1976) [10], and formulated an objective function to minimize the average cost over the expected range of parametric uncertainty, as presented by Equation (2).

$$\begin{aligned} \min_{u,des} \quad & E\{C(x, u, des, \theta)\} \\ s.t. \quad & \max_{\theta \in \Theta} \quad g_i(x, u, des, \theta) \leq 0, \quad i = 1, 2, \ldots, t \end{aligned} \tag{2}$$

where the expected cost function is defined the joint probability distribution of the parameter set θ. Equation (2) requires solving infinite nonlinear programming (NLP) problems. Grossmann and Sargent (1978) [9] proposed an efficient solution procedure for a special case of Equation (2), where each constraint g_i is monotonic in θ, through discretization of the problem over the parameter space. However, solving the NLP problem at a finite number of θ realizations does not ensure the feasibility of the design. This issue was addressed by Halemane and Grossmann (1983) [11] through reformulating an equivalent design feasibility constraint as presented by Equation (3).

$$\max_{\theta \in \Theta} \min_{u \in U} \max_{i \in I} g_i(x, u, des, \theta) \leq 0 \tag{3}$$

The max-min-max problem in Equation (3) mathematically expresses the feasibility question "For all the uncertainty realizations Θ, does there exist a control action u such that the constraint set g is feasible?". Equation (3) was employed in a multiperiod design optimization problem, where the deterministic uncertain parameter θ was allowed to vary within a prespecified range [11]. The feasibility constraint then laid the foundation for the concept of feasibility index, F, proposed by Swaney and Grossmann (1985) [12], as given by Equation (4).

$$
\begin{aligned}
F = \max \quad & \delta \\
s.t. \quad & \max_{\theta \in \Theta} \min_{u \in U} \max_{i \in I} g_i(x, u, des, \theta) \leq 0 \\
& T(\delta) = \{\theta \mid (\theta^{nom} - \delta\Delta\theta^-) \leq \theta \leq \theta \mid (\theta^{nom} + \delta\Delta\theta^+\}
\end{aligned} \tag{4}
$$

where T is the hyperrectangle for the uncertain parameters, δ is the scaled parameter deviation, and the superscript *nom* denotes nominal conditions. Equation (4) is the first significant attempt to quantify the degree of flexibility of a process design, and has been exploited by numerous studies on design optimization and process operability. However, Equation (4) constitutes a nondifferentiable global optimization problem and is still quite challenging to solve. Therefore, it requires simplifying assumptions and approximations to maintain a tractable problem. Swaney and Grossmann (1985) [13] introduced a heuristic vertex search method and an implicit enumeration scheme for the special case where the critical uncertainty realizations are assumed to lie at the vertices of the hyperrectangle $T(\delta)$. Clearly, this assumption fails to hold when the feasible space of the design problem is non-convex. Grossmann and Floudas (1987) [14] relaxed this assumption by developing a mixed-integer nonlinear programming (MINLP) problem for the feasibility test presented by Equation (3). They further proposed an active constraint strategy for the solution of the resulting MINLP. The mixed-integer formulation also provides a systematic approach to consider all possible critical uncertainty realizations without exhaustive enumeration. The proposed formulation was used for synthesis of a heat exchanger network with uncertain stream flow rates and temperatures [15]. The case of linear constraints reduces to an MILP problem, for which global solution is attainable by standard branch and bound enumeration techniques [14,16,17]. Bansal et al. (2000) [18] developed a computationally efficient theory and algorithm based on multiparametric programming techniques for this special case of flexibility analysis problems. The authors derived explicit expressions for the flexibility index as explicit functions of the continuous design variables. Pistikopoulos and Grossmann (1988a, 1988b, 1988c) used the flexibility test with linear constraints for optimal retrofit design [19–22] and redesign under infeasible nominal uncertainties [23]. Although these approaches are effective and promising to handle the design uncertainty, they require solving nested optimization problems, which poses a major challenge to solve complex and large-scale problems in a reasonable time. Raspanti et al. (2000) [24] proposed replacing the complementarity conditions of the lower level optimization problems with a well-behaved, smoothed nonlinear equality constraints, namely Kreisselmeier and Steinhauser function [25] and Chen and Mangasarian smoothing function [26].

One of the common assumptions in these approaches is the known bounds of the uncertainties, which is rarely the case in real world industrial applications. Pistikopoulos and Mazzuchi (1990) [27] and Straub and Grossmann (1990, 1993) [28,29] extended the flexibility test by assuming a probability distribution model for the parameter uncertainty, which improved the economic performance of the design optimization problem by addressing the "conservativeness" of the solution.

Another common assumption of these approaches is the steady-state operation of the plant design, which creates a significant limitation on the applicability of the methodologies. Although steady-state assumption holds true for the dominant life cycle of the plant operation, design optimization problem may fail to ensure the operability under transient behaviors such as startup or shutdown and transitions between different operating conditions. Dimitriadis and Pistikopoulos (1995) [30] proposed a dynamic feasibility index for the systems that are described by differential algebraic equations (DAE) subject to time-varying constraints. However, the time-dependent uncertainty in their formulation dictates to solve infinitely many dynamic optimization problems. Therefore, the authors assumed that the critical scenarios of uncertainties are known and lie on the vertices of the time-varying uncertainty space, similar to Swaney and Grossmann (1985) [12]. The simplifying assumption reduced the problem to the form given by Equation (5).

$$
\begin{aligned}
DF(des) = \max_{\delta, u(t), t} \quad & \delta \\
s.t. \quad & \dot{x} = f(x(t), u(t), des, \theta(t), t), \quad x(0) = x_0 \\
& g(x(t), u(t), des, \theta(t), t) \leq 0 \\
& \theta(t) = \theta^N(t) + \delta \Delta \theta^c(t) \\
& \delta \geq 0, \quad \underline{u}(t) \leq u(t) \leq \overline{u}(t)
\end{aligned}
\tag{5}
$$

where the time dependence of the variables constitutes a dynamic optimization problem, and the solution was determined by control vector parameterization techniques [30]. Dynamic flexibility has been widely used in numerous design optimization applications including batch processes [31], separation systems [32–36], reaction systems [37], and heat exchanger network synthesis [38–40].

The dynamic assessment of the plant feasibility under uncertainty has been also studied through exploiting the multiperiod design optimization formulation proposed by Halemane and Grossmann (1983) [11]. Varvarezos et al. (1992) [41] implemented an outer-approximation approach to solve the multiperiod multiproduct batch plant problems operating with single product campaigns, which was formulated as an MINLP. Pistikopoulos and Ierapetritou (1995) [42] considered stochastic process uncertainty and proposed a two-stage decomposition that can handle convex nonlinear problems.

As presented in this section, the early studies on integrated design optimization have primarily focused on (i) investigating the range of operation (flexibility) of a nominal design configuration under foreseeable conditions, and (ii) determining the "best" possible trade-off between the investment cost and the capability of handling variations in the internal and external operating conditions. These studies mostly considered open loop processes, under the traditional assumption that controller design is a sequential task to process design. However, most processes in industry are operated in closed loop, and the controller schemes inherently alter the process dynamics, rendering the open loop flexibility analyses of lesser relevance. In other words, an "attainable" operating point according to open loop flexibility analysis may actually be an infeasible point in closed loop. Realizing the shortcomings of open loop flexibility analyses, researchers began investigating the "controllability" of process systems, and the interdependence of process control and design decisions. In the following section, we present a retrospective background on the integration of process control in the design optimization problem.

3. Integration of Process Control in Design Optimization

The initial efforts towards the integration of process control and design problems established a fundamental understanding on the interdependence of the two decision making mechanisms. The most pronounced school of thought in the early years to evaluate the controllability of the process design is "dynamic resilience", as conceptually defined by Morari (1983a, 1983b) [43,44].

Morari (1983) [43] described dynamic resilience as "the ability of the plant to move fast and smoothly from one operating condition to another and to deal effectively with disturbances". This depiction implies that there is not a clear-cut distinction between flexibility, which was discussed in Section 2, and resilience. However, Grossmann and Morari (1983) [45] pointed out the main difference as "resiliency refers to the maintenance of satisfactory performance despite adverse conditions while flexibility is the ability to handle alternate (desirable) operating conditions". This distinction is the primary motive for most of the flexibility analyses to study steady-state operations, while the resilience deals with the dynamic operations, as we will discuss in this section.

Dynamic resilience, as described by Morari (1983) [43], aims to find the "perfect controller" that is allowed by the physical limitations of the system to assess the controllability of the process by using the internal model control (IMC) structure. The proposed technique decomposes the system transfer function $\tilde{G}$ into (i) a non-singular matrix $\tilde{G}_-$ to design the perfect controller $\tilde{G}_-^{-1}$, and (ii) a singular matrix $\tilde{G}_+$ to generate dynamic resilience indices based on (i) bounds on control variables, (ii) presence of right half plane transmission zeroes, (iii) presence of time delays, and (iv) plant-model mismatch. The proposed indices were used to improve the operability of numerous process, including heat integrated reactor networks [46–48], separation systems [49], heat exchanger networks [50].

Among the four aforementioned resilience indices, Perkins and Wong (1985) [51] studied the last two by adapting the "functional controllability" theorem proposed by Rosenbrock (1970) [52]. The authors further define a system to be functionally controllable if there exists a manipulated action $u(t)$ that can generate any process output $y(t)$ at any time t. Psarris and Floudas studied the dynamic resilience and functional controllability of multiple input multiple output (MIMO) closed-loop systems with time delays [53–55], and transmission zeroes [54,55]. Barton et al. (1991) [56] investigated the open loop process indicators, namely minimum singular value and right half plane zeroes, to assess the interactions between different design configurations and their operability with the best possible control configurations.

In the context of simultaneously assessing the process controllability in process design, one of the first significant contributions is the "back-off approach" introduced by Narraway et al. (1991) [57]. Narraway and Perkins (1994) [58] used this approach to systematically assess the trade-offs between all possible controlled and manipulated variable pairs in a mixed-integer formulation. Bahri et al. (1995) [59] employed the back-off approach to handle process uncertainties in an optimal control problem. The proposed approach is applicable to design linear and mildly nonlinear processes, and relies on three key steps, namely (i) perform a steady-state nonlinear process optimization, (ii) linearize the process at the optimum point, and (iii) "back-off" from the optimal solution by some distance to ensure the feasibility of the operation under some structured disturbance profile. The proposed approach was shown to be effective to select between alternative flowsheets as well as alternative control structures.

With the burgeoning interest in exploring the simultaneous design and control problem, the International Federation of Automatic Control (IFAC) organized the first workshop on "Interactions between Process Design and Process Control" in the Center for Process Systems Engineering at Imperial College London in 1992. The workshop laid the groundwork for a plethora of approaches with a wide range of diversity. Walsh and Perkins (1992) [60] implemented a PI loop in the flexibility analysis, where the input–output loop is selected by an exhaustive screening procedure. Luyben and Floudas (1992) [61] formulated a multiobjective MINLP problem to simultaneously consider the disturbance rejection capacity of the control loop through disturbance condition number and relative gain array to evaluate the interactions between the inputs and outputs of a MIMO system, while designing the process. Shah et al. (1992) [62] used the State-Task Network (STN) representation [63] to simultaneously consider the scheduling and design problems in a batch plant. Thomaidis and Pistikopoulos (1992) [64] introduced a framework to consider the design problem simultaneously with (i) the process flexibility through stochastic flexibility index, (ii) the effect of equipment failures to the overall performance by combined flexibility-reliability index, and (iii) the impact of equipment availability by combined flexibility-reliability index. These aforementioned novel approaches were shown to be promising concepts and techniques to address multiple facets of operational decisions simultaneously with the process design problem. As a result, succeeding studies after this workshop expanded these techniques and branched out to explore further opportunities.

Integrating PI controllers in the design optimization problem was one of the prominent outcomes of the workshop and became the most attractive option for the following research. The literature on PI controllers was already abundant and well-established by the time. Moreover, the explicit form of the controller structure made the integration relatively easy and intuitive, which significantly accelerated the research in closed-loop design optimization. Walsh and Perkins (1994) [65] presented an integrated

PI control scheme and process design for wastewater neutralization. Although the proposed approach was effective for the SISO process, it was reported that it entails further challenges for more complex processes. One major drawback of PI control is its inability to tackle MIMO systems without any advanced modifications in the feedback loop structure. Narraway and Perkins (1993, 1994) [58,66] developed an MILP-based formulation to systematically evaluate the economic performance of every input–output pair combination. Luyben and Floudas (1994a, 1994b) [67,68] adapted a similar approach in a multiobjective framework to determine the best performing input–output pair based on the controllability indices introduced by them, earlier (1992) [61]. The proposed framework was showcased on the design of a heat integrated distillation system [67] and a reactor-separator-recycle system [68]. Mohideen et al. (1996) [32] formulated a multiperiod design and control problem to account for the dynamic variations in the operation, while including the input–output pairing superstructure in the problem. Moreover, the authors used the flexibility index to account for the uncertain parameters in the model and presented a decomposition algorithm for the resulting complex problem. Bansal et al. (2000) [69] constructed a similar formulation as a mixed-integer dynamic optimization (MIDO) problem, which was solved by a Generalized Benders Decomposition (GBD)-based algorithm. The MIDO formulation was presented as follows.

$$
\begin{aligned}
\min_{u,des} \quad & \sum_{i \in NS} w_i C\left(\dot{x}^i(t), x^i(t), u^i(t), des^i\right) \\
s.t. \quad & \dot{x}^i(t) = h_d\left(x^i(t), u^i(t), des^i, \theta^i, t\right), x(t) = x_0 \\
& y^i(t) = h_a\left(x^i(t), u^i(t), des^i, \theta^i, t\right) \\
& g\left(\dot{x}^i(t), x^i(t), y^i(t), u^i(t), des^i, \theta^i, t\right) \leq 0
\end{aligned}
\tag{6}
$$

where w_i is the discrete probability of a scenario i and NS is the discretized set of scenarios. The discretization of uncertainty in the process was first proposed by Grossmann and Sargent (1978) [9].

Although the aforementioned PI-based design and control frameworks are applicable on nonlinear processes, the range of operability is usually limited due to the mismatch between the nonlinear process model and the linearized control model. Ricardez-Sandoval et al. (2008, 2009) [70,71] used robust control tools and the back-off approach to integrate PI control and ensure its stability while solving the design optimization problem. The proposed approach was also tested against the Tennessee Eastman Process [72]. The back-off approach was later generalized for control structure selection in nonlinear processes by Kookos and Perkins (2016) [73]. Ricardez-Sandoval & co-workers have extensively studied back-off approach for simultaneous process design and control under uncertainty [74–76].

One main limitation of integrating PI control in the design optimization in a dynamic formulation is the increasing problem size and complexity. Kookos and Perkins (2001) [77] developed an algorithm for the integrated PI control and design optimization problem, where the size of the search space was reduced systematically in each successive iteration. Malcolm et al. (2007) [78] proposed an "embedded control optimization" procedure, where the authors introduced a two-stage decomposition scheme that approximates the complete integrated problem. The proposed approach reduced the problem size and complexity, and was showcased on larger scale problems including a reactor-separator system [79].

Apart from the inability to naturally handle MIMO systems, PI controllers do not explicitly account for any process constraints stemming from operational, environmental, and safety limitations. Model predictive control (MPC) overcomes these shortcomings by postulating a constrained dynamic optimization problem subject to an explicit model of the process [80]. One of the first remarkable efforts to integrate an MPC scheme in a nonlinear design problem was published by Brengel and Seider (1992) [81].

Here, the authors postulate a bi-level optimization problem, where the *leader* has an economic objective, while the *follower* is the MPC formulation, as presented by Equation (7).

$$\begin{aligned}
\min_{des} \quad & C_{des}\big(des\big) + \kappa C_{\kappa}\big(x(t), y(t), u(t), des, \theta(t)\big) \\
s.t. \quad & f_{des}\big(des, \theta(t)\big) = 0 \\
& g_{des}\big(des, \theta(t)\big) \leq 0 \\
& \min_{u(t)} \quad C_u\big(x(t), y(t), u(t), des, \theta(t)\big) \\
& \quad s.t. \quad \dot{x} = f_u\big(x(t), y(t), u(t), des, \theta(t)\big) \\
& \qquad\qquad g_u\big(x(t), y(t), u(t), des, \theta(t)\big) = 0 \\
& \qquad\qquad h_u\big(x(t), y(t), u(t), des, \theta(t)\big) \leq 0
\end{aligned} \tag{7}$$

where κ is the design and control integration parameter that scales the trade-off between the controllability of the system and the investment cost. The bi-level problem presented in Equation (7) is challenging to solve without appealing to simplifications. Therefore, the authors proposed replacing the follower problem by complementary slackness equations. However, the solution strategy was still intractable for more complex systems due to the numerical calculation of the second derivatives [81]. As a consequence, integration of the MPC scheme in the design optimization had been rather limited in the literature for almost a decade, until the invention of multiparametric MPC (mpMPC/explicit MPC).

Bemporad et al. (2002) [82] proposed formulating the MPC problem as an explicit function of the initial conditions of the system. This novel strategy allowed for deriving piecewise affine explicit control laws by treating the initial conditions as parameters. The proposed approach formulated the explicit MPC problem as presented by Equation (8).

$$\begin{aligned}
u_t(\theta) = \quad & \arg\min_{u_t} \|x_N\|_P^2 + \sum_{t=1}^{N-1} \|x_t\|_Q^2 + \sum_{t=1}^{N-1} \|y_t - y_t^{sp}\|_{QR}^2 + \sum_{t=0}^{M-1} \|u_t - u_t^{sp}\|_R^2 + \sum_{t=0}^{M-1} \|\Delta u_t\|_{R1}^2 \\
s.t. \quad & x_{t+1} = Ax_t + Bu_t + Cd_t, \quad y_t = Dx_t + Eu_t + Fd_t \\
& \underline{x}_t \leq x_t \leq \overline{x}_t, \quad \underline{y}_t \leq y_t \leq \overline{y}_t, \quad \underline{u}_t \leq u_t \leq \overline{u}_t, \quad \underline{\Delta u}_t \leq \Delta u_t \leq \overline{\Delta u}_t, \quad \underline{d}_t \leq d_t \leq \overline{d}_t \\
& \theta = [x_{t=0}, u_{t=-1}, d_t, y_t^{sp}, u_t^{sp}]^T
\end{aligned} \tag{8}$$

where N is the prediction horizon, M is the output horizon, superscript sp denotes set point, Q, QR, R, and $R1$ are the corresponding weight matrices determined by tuning, P is calculated by discrete algebraic Riccati equation, and $\|\cdot\|_\psi$ denotes weighted vector norm with a weight matrix ψ. Different than conventional MPC, Equation (8) formulates the optimal control problem exactly and completely offline as a function of the set of parameters θ. The solution of this problem can be determined by multiparametric programming techniques, which express the solution space as a piecewise affine function, as presented by Equation (9).

$$\begin{aligned}
u_t(\theta) =& K_n\theta + r_n, \quad \forall \theta \in CR_n \\
CR_n :=& \{\theta \in \Theta \mid CR^A\theta \leq CR^b\}, \quad \forall n \in \{1, 2, \ldots, NC\}
\end{aligned} \tag{9}$$

where CR_n is referred as a critical region and it is the active polyhedral partition of the feasible parameter space, Θ is a closed and bounded set, and NC is the number of critical regions.

The control law given by Equation (9) reduces the complexity of solving an online optimization problem to a simple look-up table algorithm (also known as point location problem) and function evaluation, all of which are affine operations. Hence, the complexity of implementing an MPC scheme is similar to that of a PI controller.

Sakizlis et al. (2003) [83] exploited the explicit nature of the mpMPC solution in the context of design and control integration. The authors formulated a bi-level mixed-integer dynamic optimization problem similar to Equation (7), where the leader accounted for the investment and operating costs in the objective function subject to the dynamic high-fidelity model, and the follower MPC problem was substituted by the affine control law Equation (9). The proposed formulation offered an elegant and systematic methodology to reduce the complexity of the bi-level Equation (7) into a single level dynamic optimization problem. However, the solution strategy still required repetitive linearizations and solving a multiparametric programming problem at every iteration, which can be restrictive for large-scale complex problems. Diangelakis et al. (2017) [84] alleviated that limitation by deriving a "design dependent offline controller", which allowed for solving a single MIDO problem after integrating the control law in the high-fidelity model. Eliminating the linearization step and formulating a single synergistic design and control problem also improved the economic performance of the resulting process compared to the approach proposed by Sakizlis et al. (2003) [83]. The proposed formulation was also showcased on a tank, a continuous stirred tank reactor, and a residential scale combined heat and power unit. The cost effectiveness of the MPC integrated optimal design was also reported to be superior than PI integrated approaches in the literature. Diangelakis and Pistikopoulos (2017) [85] reported that the mpMPC integrated optimal combined heat and power unit operated more fuel efficient in closed loop than PI integrated design. Similarly, Sanchez-Sanchez and Ricardez-Sandoval (2013) [86] showcased a system of CSTRs, where the MPC integrated framework reduced both the operating and the investment costs compared to the PI control integrated approach.

One common aspect of the studies on simultaneous design and control optimization is the assumption that the process will be operated around the same steady-state point throughout the entire life cycle of the plant. However, the external plant conditions, such as market conditions, may dictate a considerably wider operating region with multiple steady-state points [1]. The increasing competition among the businesses impacts the volatility of the market, which creates rapid fluctuations in the energy and raw material prices as well as their availability. Moreover, the demand rate on the product is also subject to considerable variations during the plant operation. Therefore, it is clear that there exists a "best" operating strategy under the knowledge available to the operator, which necessitates the operability of the plant across a wider range. For example, high production rates may be less profitable during the night time because of increased energy prices and hence, operating the energy intensive processes during the daytime may reduce the operating costs. This indicates that the operating level of a processing unit might vary drastically by the choice of the operator. However, the integrated design and control frameworks discussed in this section usually assume a single operating point around which a controllability and flexibility analysis is conducted. Consequently, these frameworks do not attempt to provide any means of guaranteeing the operability of the process at different regions. In the next section, we will discuss several approaches that account for multiple operating regions in a plant, and their scheduling during the operational optimization.

4. Towards the Grand Unification of Process Design, Scheduling, and Control

Process design, scheduling, and control problems are traditionally constructed to address different objectives and they span widely different time scales. In a nutshell, the plant design problem dictates the capacity of processing and it usually comprises the most uncertainty due to its years long lifecycle. The scheduling problem addresses the allocation of the resources and time, as well as the operating level of processing units and their maintenance based on some economic criteria over days/months long horizons. Lastly, the control problem maintains the performance of the plant, while satisfying any physical limitations such as the environmental and safety constraints. The discrepancy in the objectives and time scales creates a challenging problem to systematically evaluate and determine the optimal trade-off between different decision makers.

Process scheduling is more critical in batch operations than continuous operations, as the former are inherently dynamically operated. Accordingly, the initial efforts focused primarily on the batch processes for the integration of the operational optimization and design problems. Birewar and Grossmann (1989) [87] formulated NLP models to incorporate the scheduling decisions in the batch sizing and timing problem in a multiproduct plant for unlimited intermediate storage and zero wait policies. Shah et al. (1992) [62] tackled a similar problem by using the STN representation. White et al. (1996) [88] investigated the switchability of continuous processes between different operating points through formulating an optimal control problem that accounts for the terminal criteria and path constraints within a range of design parameters. Bhatia and Biegler (1996, 1997) [89,90] formulated a dynamic optimization problem, where an economic objective function was subject to a dynamic high-fidelity model of the process described by differential algebraic system of equations. The authors proposed a solution strategy based on discretizing the process model by orthogonal collocation over finite elements, followed by solving the resulting NLP by using a standard solver. The proposed modeling and solution strategy was shown to be promising to satisfy the path constraints, which is a crucial benefit for dynamic systems. Terrazas-Moreno et al. (2008) [2] extended this integration approach to account for the binary decisions in the scheduling problem by formulating a MIDO. Similar to Bhatia and Biegler (1996, 1997) [89,90], the authors first discretized the problem by orthogonal collocation, followed by solving the resulting MINLP.

The early studies that explore the interactions between the scheduling and process control decisions have a significant role in shaping today's approaches for the integrated design optimization problem. In their excellent review article, Baldea and Harjunkoski (2014) [91] classified these attempts to integrate the scheduling and control decisions as (i) "top-down approaches", where the process dynamics and control elements are incorporated in a scheduling skeleton, and (ii) "bottom-up approaches", where the process economics are implemented in the plant-wide control decisions.

In terms of characterizing the transitions between different products in a single operating unit, Mahadevan et al. (2002) [92] introduced a unique "top-down" perspective on the operational optimization problem, revealing that a simultaneous approach on the scheduling and control problem can identify and eliminate the fundamental limiting behavior during the transitions, as showcased on a polymer grade transition process. However, the presented approach requires case specific heuristic decisions to select the "best" fitting scheduling and control configuration and hence, it is not suitable for different applications in the general sense. Chatzidoukas et al. (2003) [93] studied a similar polymerization reactor, and formulated a MIDO problem to determine the time optimal transition between different polymer grades and best performing control structure simultaneously. Flores-Tlacuahuac and Grossmann (2006) [94] introduced a monolithic approach on a multiproduct cyclic CSTR, where the profit was maximized by manipulating the production sequence, transition times, production rates, length of processing times, and amounts manufactured of each product. In contrast to the earlier studies [92,93], the authors focused on the manipulated actions rather than the optimal control configuration. They formulated a MIDO problem, which was solved by discretization of the differential algebraic equations by orthogonal collocation on finite elements followed by solving the resulting MINLP. The presented approach has been extensively studied in the following years to broaden its scope and effectiveness. Terrazas-Moreno et al. (2007) [95] applied this approach on two industrial polymerization reactors. Terrazas-Moreno et al. (2008) [2] formulated a design optimization problem accounting for the scheduling and open loop control trajectories using this approach. Flores-Tlacuahuac and Grossmann (2010, 2011) extended the formulation to partial differential equation systems, and showcased on tubular reactors with single [96] and multiple production lines [97].

This monolithic approach usually generates open loop control trajectories, i.e., no feedback loop is assumed to develop the input and output profiles. However, the processing units are subject to internal process disturbances, and the mismatch between the process and the model leads to deviations in the targeted operations. Zhuge and Ierapetritou (2012) [98] implemented the monolithic approach in closed loop, where the authors initiate a readjustment procedure to solve the integrated problem online if the states deviate from their reference trajectories. This approach does not completely resolve the issue of handling the process disturbances or the process/model mismatch; however, it was shown to mitigate these concerns to a great extent. Gutiérrez-Limón et al. (2014) [99] also implemented a similar closed-loop strategy with a nonlinear model predictive control scheme, while extending the scope of the problem statement to account for an extended horizon production policy. However, both approaches require solving a complex and large-scale MINLP problem at the time steps of the controller, which makes it unsuitable for the processes with fast dynamics.

Low-order representation of fast process dynamics in the scheduling problem has been an effective approach to reduce the computational burden of solving complex optimization problems. Du et al. (2015) [100] proposed a time scale-bridging model that describes the closed-loop input–output behavior of a process in the scheduling formulation, postulated as a MIDO problem. The low-order representation also maintains the stability of the process in the existence of process/model mismatch and handles disturbances. Baldea et al. (2015) [101] extended this approach to MPC governed systems.

Burnak et al. (2018) [102] also addressed the online computational burden of "top-down" approaches by developing a multiparametric programming-based approach, where the authors explicitly mapped (i) the closed-loop dynamic process behavior in a "control-aware" scheduling problem, and (ii) the continuous and binary scheduling level decisions such as the operating level and operational mode of the system in a "schedule-aware" MPC scheme (iii) to yield the optimal operational decisions. The offline nature of the integrated scheduling and control scheme allows for determining the feasible operating space prior to actualizing the operation. Furthermore, reducing the problem complexity from solving online optimization problems to a simple look-up table and affine function evaluation, the framework is well-suited for fast process dynamics. Charitopoulos et al. (2019) [103] employed a similar multiparametric programming approach to include the planning decisions in their framework.

In the "bottom-up" approaches, on the other hand, incorporating the economic objectives in the plant control structures has been perceived as the key for seamless integration of scheduling and control. For this purpose, MPC formulations provide the flexibility to account for a spectrum of objectives in the control level due to their optimization-based structures. Loeblein and Perkins (1999) [104] presented an economic analysis of unconstrained MPC scheme operating under constrained systems. The authors determined the most cost-effective model predictive regulatory control structure by using the back-off approach to satisfy the constraints. Zanin et al. (2002) [105] addressed the discrepancy between the real-time optimization (RTO) and control layers by incorporating the economic optimization problem in the controller and feeding the same piece of information in both layers. The proposed formulation diminishes the discrepancy between the decision layers to yield more economical operations, but the resulting control scheme does not guarantee the stability of the process for the entirety of operations. Rawlings and Amrit (2009) [106] developed asymptotic stability criteria by formulating the so-called "economic MPC" (or EMPC), where the objective function of the MPC is designed to minimize the operational costs instead of maintaining the steady state of the process. This approach aims to replace the conventional two-layer structure with RTO and dynamic regulatory control by a single control layer, where the economic optimization and process regulation are conducted simultaneously. Amrit et al. (2011) [107] further extended the stability criteria by (i) imposing a region constraint on the terminal state instead of a point constraint, and (ii) adding a penalty on the terminal state to the regulator cost.

Similar to the monolithic "top-down" scheduling and control approach, EMPC has been shown to be too complex to be solved in the control time steps. This limitation has led the researchers to develop decomposition algorithms for faster computational times. Würth et al. (2011) [108] proposed a decomposition framework for the single layer dynamic RTO formulation, where the slow trends and process uncertainty is handled in the upper layer, while the lower layer accounts for the fast disturbances acting on the process. Ellis and Christofides (2014) [109] focused on selecting a suitable input configuration for such two-layered dynamic RTO structures such that the asymptotic stability is guaranteed. Jamaludin and Swartz (2017) [110] and Li and Swartz (2019) [111] employed a convex MPC problem in the lower level regulatory control, which enabled its exact substitution with KKT optimality conditions. Simkoff and Baldea (2019) [112] used the same substitution strategy on a production scheduling problem.

Design optimization accounting for the scheduling and control decisions with closed-loop implementation is relatively recent in the literature. Patil et al. (2015) [3] modeled the product transitions in design optimization, while maintaining the stability of the closed-loop system governed by a PI control scheme. The authors formulated an MINLP similar to Equation (6) with the contribution of the criterion, $eig(A_i^z(x_{lin})) < 0$, which enforces the stability of the linearized states for all products i in a multiproduct unit under all critical scenarios z. Due to the linearization of the controllers around the operating point, this approach requires repetitive identification of the states at every optimization iteration. Koller and Ricardez-Sandoval (2017) [4] improved this approach by applying orthogonal collocation on finite elements on the integrated problem, and Koller et al. (2018) [5] employed the back-off method to satisfy the constraints under uncertainty by using Monte Carlo sampling techniques to determine the back-off terms.

Recently, Burnak et al. (2019) [6] introduced a multiparametric programming-based theory and framework for the integration of process design, scheduling, and control. The authors derived offline design dependent control and scheduling schemes that can be incorporated in a MIDO formulation in a multi-level fashion, as presented by Equation (10).

$$
\begin{aligned}
\min_{u,s,des} \quad & \int_0^{\tau} C(x(t), y(t), u(t), s(t), des, d(t))dt \\
s.t. \quad & \dot{x}(t) = f(x(t), y(t), u(t), s(t), des, d(t), t) \\
& \underline{y} \leq y(t) = g(x(t), y(t), u(t), s(t), des, d(t), t) \leq \overline{y} \\
& \underline{x} \leq x(t) \leq \overline{x}, \quad \underline{des} \leq des \leq \overline{des}, \quad \underline{d} \leq d(t) \leq \overline{d} \\
& s_t(\theta_s) = \arg\min_{s} \quad \sum_{t_s \in N_s} C_s(x_{t_s}, y_{t_s}, s_{t_s}, des, d_{t_s}) \\
& \qquad s.t. \quad \underline{x}_{t_s} \leq x_{t_s+1} = A_{t_s}x_{t_s} + B_{t_s}s_{t_s} + C_{t_s}d_{t_s} \leq \overline{x}_{t_s} \\
& \qquad \qquad \underline{y}_{t_s} \leq y_{t_s} = D_{t_s}x_{t_s} + E_{t_s}s_{t_s} + F_{t_s}d_{t_s} \leq \overline{y}_{t_s} \\
& \qquad \qquad \underline{s}_{t_s} \leq s_{t_s} \leq \overline{s}_{t_s}, \quad \underline{d}_{t_s} \leq d_{t_s} \leq \overline{d}_{t_s} \\
& \qquad \qquad \underline{\theta}_s \leq \theta_s = [x_{t_s=0}^T, y_{t_s=0}^T, d_{t_s}, des]^T \leq \overline{\theta}_s \\
& u_t(\theta_c) = \arg\min_{c} \quad \sum_{t_c \in N_c} C_c(x_{t_c}, y_{t_c}, u_{t_c}, des, d_{t_c}) \\
& \qquad s.t. \quad \underline{x}_{t_c} \leq x_{t_c+1} = A_{t_c}x_{t_c} + B_{t_c}u_{t_c} + C_{t_c}d_{t_c} \leq \overline{x}_{t_c} \\
& \qquad \qquad \underline{y}_{t_c} \leq y_{t_c} = D_{t_c}x_{t_c} + E_{t_c}u_{t_c} + F_{t_c}d_{t_c} \leq \overline{y}_{t_c} \\
& \qquad \qquad \underline{u}_{t_c} \leq u_{t_c} \leq \overline{u}_{t_c}, \quad \underline{d}_{t_c} \leq d_{t_c} \leq \overline{d}_{t_c} \\
& \qquad \qquad \underline{\theta}_c \leq \theta_c = [x_{t_c=0}^T, y_{t_c=0}^T, d_{t_c}, des]^T \leq \overline{\theta}_c
\end{aligned}
\tag{10}
$$

where s and u denote the scheduling and control decisions, respectively. Note that the proposed formulation postulates explicit expressions for the scheduling and control strategies as functions of a set of parameters, θ, which includes the design of the process. The design dependence of the operational strategies allows for their direct integration in the MIDO formulation. The postulated formulation has two main benefits, (i) due to the explicit form of the follower problems, the multi-level MIDO problem is reduced to a single level, and (ii) only the design variables are left as the degrees of freedom of the problem, since the remaining are determined as a function of the design.

5. Current Challenges and Future Directions

The PSE community has achieved unequivocally remarkable progress in realizing and advancing the set goals of Professor Sargent on systematic design optimization in five decades. Today, using design optimization tools to at least some extent has long become the standard practice in many industries. Commercial modeling and simulation software tools such as gPROMS (https://www.psenterprise.com/products/gproms) and Aspen Plus Dynamics (https://www.aspentech.com/en/products/pages/aspen-plus-dynamics) have been featuring robust and efficient solvers for dynamic optimization problems for a few years. Despite these milestones in PSE, we still must make significant assumptions and simplifications regarding the operational decisions in the process design phase, even though the impact of their interdependence on process economics and operability has been articulated in numerous studies. Hence, the academia still needs to mature the theoretical foundations and the applicability of unified design optimization approaches before it gains wide industrial recognition. Here, we discuss some of the bottlenecks and potential directions to improve the state-of-the-art for industrial practice.

5.1. The Need for an Industrial Benchmark Problem

As we have presented in this paper, there is a plethora of proposed modeling techniques and solution approaches for the next generation unified design optimization problems. Therefore, it is clear that we need a generally accepted benchmark problem, preferably in industrial scale, to validate the effectiveness of proposed methodologies. The PSE community has benefited greatly from such standardized problems, such as the famous Tennessee Eastman Process detailed by Downs and Vogel (1993) [113] for process control studies. We believe that a well-defined problem will clarify the objectives in unified design optimization and accelerate the research towards industrial expectations. The problem should describe at least the following.

1. *A high-fidelity model that describes the dynamics of the process*. The model should feature appropriate design variables to exhibit the dynamic consequences of scaling up/down the process. Furthermore, considering the reduction in capital investment that the multipurpose and multiproduct operating units provide, the process should comprise such units to examine the scheduling/design and scheduling/control trade-offs. Recent research that consider process design, scheduling, and closed-loop control problems simultaneously [3,5,6] have studied only a single processing unit, which reflects a limited fraction of the overall benefit that the grand unification can provide.
2. *Cost relations for investment, utility, and raw materials*. A functional form of the investment cost with respect to the capacity of the process is required to have standardized comparable results. Also, utility costs and raw materials may vary significantly, which inevitably impacts the optimal scheduling decisions. For instance, grid electricity costs are known to exhibit considerable differences during the day and night times. Thus, operational loads in energy intensive processes may fluctuate heavily. The impact of such changes in operating levels on design and control decisions were discussed in Section 3.

3. *Product demand and availability of the utility, raw materials, and operating units over a time horizon*. Production allocation and timing is a key aspect of scheduling problem, which are heavily dictated by the product demand and availability of resources. However, it is not a trivial practice to estimate the future of these quantities. Therefore, probability distributions of these components will be beneficial to determine their expected values, while being able to take into account their worst-case scenarios.

5.2. Robust Advanced Control and Scheduling Strategies

Incorporation of advanced control schemes seamlessly in the design optimization problem requires the controller to capture the dynamics of the process for the entire range of design variables. Burnak et al. (2019) [6] attempted to approximately model the design configuration as a right-hand uncertainty in the constraint set, validated by closed-loop simulations and closed-loop MIDO problems. However, the design variables impose uncertainty in the left-hand side of the constraints, as well as the nonlinear and bilinear terms in the objective function. Therefore, robust control strategies need to be developed for accurate predictions of future states in the control level prior to the realization of the design, and to guarantee the stability of the closed-loop operations in simultaneous approaches.

Analogously, scheduling schemes should be robustified in the design optimization to minimize the rescheduling due to unexpected disruptive events, such as unit failure, drastic changes in product demand rate and raw material availability. Excluding these events in the scheduling scheme may result in steep changes in the target operation, and thus unattainable set points for the controller.

5.3. Considering Flowsheet Optimization, Process Intensification, and Modular Design Opportunities

Optimization-based plant design techniques have been used and developed for more than four decades [114,115]. These techniques postulate "superstructures" that systematically simulate and compare every combination of flowsheet possibility to determine the optimal process. More recently, superstructures have been formulated at the phenomena level to capture the fundamental relations between the mass and energy, which in turn yields intensified processes [116–122]. Such intensified processes are expected to deliver significantly increased operational efficiency and decreased unit volumes, making them very attractive options both in academia and industry [123]. This rapidly growing interest in intensified processes is one of the most pronounced directions that the PSE community has been taking. Therefore, studying these intensified processes in the context of unified design optimization will attract a wider audience from the industry. Clearly, modeling the spatial (synthesis/intensification) and temporal (scheduling/control) decisions simultaneously in a single problem formulation will capture even more synergistic interactions, which will increase the process profitability.

Furthermore, the researchers studying process intensification can benefit from the tools and methodologies on unification of design, scheduling, and control. Baldea (2015) [124] reported a theoretical justification for the loss of control degrees of freedom due to process intensification, which poses a significant limitation on intensification activities. Tian and Pistikopoulos (2019) [125] and Dias and Ierapetritou (2019) [126] discuss the limitations on the operability of such intensified systems and potential directions to overcome these limitations in their excellent review papers. The researchers on process intensification technologies can adopt the techniques, ranging from steady-state and dynamic flexibility to integration of scheduling and control decisions, in order to address the operability issues.

5.4. Theoretical and Algorithmic Developments in MIDO

The most limiting bottleneck of the simultaneous approaches is the size of the integrated MIDO problems. The time component of the problem significantly increases the computational complexity, yielding infinitely many NP-hard problems to acquire an optimal solution profile. However, tailored algorithms can be developed by using the special structure of such integrated problems. For instance, the open loop design optimization problem is relatively simpler than the integrated MIDO, and constitutes a lower bound on the optimal solution of the overall problem. Such properties can be exploited in decomposing the MIDO into subproblems to significantly reduce the search space for faster algorithms.

5.5. Software Development

Despite the theoretical and practical advances in the unified design problem among the academia, there is no commercially available platform or a software prototype. Such a tool will make the integrated approaches more accessible to the process designers in industry who are not necessarily experts on process control and scheduling, and it will attract more researchers from different disciplines and backgrounds. Pistikopoulos et al. (2015) [127] introduced the PARametric Optimization & Control (PAROC) framework to design explicit controllers based on high-fidelity models, which can be a viable option to address the grand unification challenge [6,84,102,128,129]. However, it is clear that more progress is needed to engage a wider audience.

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