# Reduction of Complexity via Operatorial Parametric Formulations for Some Nonlinear Dynamic Problems of Biology

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## Abstract

*Dynamic models most of the time involve differential equations, which are "time-local". Such models can also be considered "globally", that is in the sense of "trajectories" in the "space-time" state. Up to adapted concepts, such a different interpretation reveals itself more flexible, namely because it allows to use various operatorial transformations whose time-local equivalent in general cannot exist and from which can result some remarkable properties. Namely, we introduce a principle of parametrizing for dynamic equations by means of such transformations. We then consider an example of bioreactor model for which we highlight how suitable time-nonlocal transformations can sometimes be used to efficiently solve some nonlinear control problems.*

## 1 Introduction

Several dynamic biological models are composed of a large number of coupled nonlinear differential equations with the particular property that some characteristic quantities are involved in many of these equations. This is typically the case for example for bioreactors equations, cell metabolism equations, etc. Such remarkable quantities are often of great significance from both the physical and mathematical points of view and so, it can seem judicious to strengthen their role in the analysis of the model by use of suitable transformations, in aim of reducing the mathematical and numerical complexity of the problem under consideration. This is the main topic of this introductive work.

The paper is organized as follows. In section 2, we introduce some basic notions relating to the so-called parametrizing of dynamic equations and highlight them by means of a simple but significant example. In section 3, we state the suitable mathematical framework for the parametrizing concept which is then developed in section 4. Finally, a consistent example is studied in section 5, which highlights how some control problems can be significantly simplified by use of suitable operatorial parametrizing of the dynamic model under consideration.

## 2 Preliminary notions and basic example

From an abstract point of view, dynamic problems can be expressed under the generic form :

$$\mathbf{\Phi}(u, x) = 0 \tag{1}$$

where $x$ is the trajectory in the state space, that is $\forall t > 0$, $x(t) \in \mathbf{X}$, and $u$ is the unknown (for example the control, some parameters, etc.), which is here considered as a function of $t$ (in some particular cases, this function can be constant), that is a trajectory in a suitable space: $\forall t > 0$, $u(t) \in \mathbf{U}$. In some particular cases, when the model (1) can be expressed explicitly under the form:

$$u = \mathbf{R}(x), \tag{2}$$

the solution of problems relating to such a model can be simplified because the unknown $u$ is straightforwardly deduced from $x$. In practice, such a simplification (which can be sometimes significant) is often "hidden" when using standard approaches relating to models (1) of the form[1]:

$$H(\partial_t)x = f(u, x). \tag{3}$$

Such approaches are indeed based on the implicit relation $x = \mathbf{F}(u)$ associated with the model (1), whose evaluation necessitates to solve (with respect to $x$) the state equation (3), which is in general a difficult task, specially when the

[1] $\partial_t$ designates the derivative time operator.

dynamic equation intrinsically generates complex and sensitive dynamic behaviors.

To illustrate the above statements, let us consider the following dynamic model[2]:

$$\ddot{x} - k\,\dot{x} - K\,x = \frac{q\,V^2}{(\alpha - x)^2}, \tag{4}$$

$$x(0) = x_0,\ \dot{x}(0) = x_1 \tag{5}$$

$$x \in \mathcal{X} \subset C^2(\mathbb{R}_t^+).$$

First, note that if we suppose that $x(t) = 0$ and $V(t) = 0\ \forall t < 0$, then the system (4,5) can be rewritten, with $a, b$ suitably chosen from $x_0$ and $x_1$:

$$\partial_t^2 x - k\,\partial_t x - K\,x = \frac{q\,V^2}{(\alpha - x)^2} + a\,\delta + b\,\delta'\ \forall t \in \mathbb{R}. \tag{6}$$

Given a transfer function $H(p) \overset{\infty}{\sim} p^{-2}$ associated to the impulse response $h$; we denote $\mathcal{H}_1 := \left[H(\partial_t) \circ \partial_t^2\right]$, $\mathcal{H}_2 := [H(\partial_t) \circ \partial_t]$, $\mathcal{H} := H(\partial_t)$. The following functional equation, deduced from (6) by composition with operator $\mathcal{H}$:

$$\mathcal{H}_1\,x - k\,\mathcal{H}_2\,x - K\,\mathcal{H}\,x = q\,\mathcal{H}_{\frac{V^2}{(\alpha-x)^2}} + a\,h + b\,\dot{h}$$

admits formal explicit solutions with respect to the unknown $u$:

- $u := V$ for control problems ($k, K, q$ are supposed to be known)
- $u := (k, K, q)^T \in \mathbb{R}^3$ for the problem of identification of the system coefficients ($V, a, b$ are supposed to be known), etc.

In general, it is not possible to express $u$ explicitly as a function of $x$, in particular because of the vectorial nature of $u(t)$ and $x(t)$ with $\dim(x(t)) > \dim(u(t))$.

However, in various non trivial cases with practical interest, it remains possible to implement some more or less complex (but explicit) transformations in a way quite similar to the previous example, in such a manner that complete or partial explicitation of the unknown $u$ under interest can be obtained from simple formal calculations. This is the topic of the present paper.

The aim of this work is not to construct some general techniques or methods, but simply to propose a mathematical framework and some basic notions to correctly state the general problem of (reduction of complexity via) parametrizing relating to problems of any nature based on models (1). For concrete implementations, functional, operatorial and numerical analysis will be used to elaborate efficient tools; this will be studied in further works.

[2]Such models are used for some MEMS with electrostatic control $V$.

## 3 Models under consideration

Let $\mathcal{U}, \mathcal{X}$ two manifolds, $\mathcal{E}$ a topological vector space and $\Phi : \mathcal{U} \times \mathcal{X} \to \mathcal{E}$ an application[3]. We consider the following abstract equation in $\mathcal{U} \times \mathcal{X}$ (the model):

$$\Phi(u, x) = 0. \tag{7}$$

We suppose that (7) is well-posed, that is for any $u \in \mathcal{U}$, there exists a unique $x \in \mathcal{X}$ such that $(u, x)$ is solution of (7), with $\mathbf{F} : u \mapsto x$ continous.

For $J : \mathcal{U} \times \mathcal{X} \to \mathbb{R}$ a given functional, we can consider, for example, the problem $\min J$ under the constraint (7):

$$\min\{J(u, x);\ (u, x) \in \mathcal{U} \times \mathcal{X},\ \Phi(u, x) = 0\}. \tag{8}$$

In the sequel, we propose to replace $u$ by an "object" $y$ with similar nature (in a sense to be precized), which will be called *parameter* and devoted to simplify the resolution of problem (8).

We make the **main hypothesis** that all the involved linear operators are realizable with reasonable cost, and so are available for formal developments. Note that the mathematical framework and notions suited to this hypothesis is presented in [4].

**Definition 1** *In the case of dynamic problems, equation (7) is said explicit when $\Phi(u, x) = \mathcal{H}x - F(u, x)$, where:*

- *$\mathcal{H}$ is an invertible integral operator[4],*
- *$F(u, .)$ is a static operator.*

When $F$ is of the form $F(u, x) = Ax + Bu$ with $A, B$ linear static operators, the model is linear. In this case, we have $(\mathcal{H} - A)x = Bu$ and, if $(\mathcal{H} - A)$ is invertible, $x = (\mathcal{H} - A)^{-1}Bu = \tilde{\mathcal{H}}u$. Thus, without loss of generality, we can suppose that linear models are solved under the form $X = \mathcal{K}u$ (with $\mathcal{K}$ linear). For this reason and under the main hypothesis, the notions introduced in the sequel are trivial in the case of linear models.

**Remark 1** *In some cases where the concrete inversion of the linear operator $\mathcal{H} - A$ could constitute a difficult problem (in other words, the main hypothesis is not satisfied), we can consider the model under the form $\mathcal{H}x = Ax + Bu$. The notions introduced in the sequel remain of course valid; but in such cases, the linear nature of the model allows a simplified statement, namely by use of some specific algebraic tools (cf. [15], [13]).*

[3]The continuity of $\Phi$ is not necessary.

[4]Possibly depending on $u$.

When it is explicit, the equation (7) can be rewritten: $x = \mathcal{H}^{-1} \circ F(u, x)$. The interest of explicit models then clearly appears when the operator $\mathcal{H}^{-1}$ is *causal* : it lies in the fact that it is in general possible to implement $t$*-local* numerical algorithm to solve the equation, under the recurrent form (cf.[4]):

$$\begin{aligned} \psi(t_{n+1}) &= K(t_n, u, \psi(t_n)), \\ x(t_n) &= M(\psi(t_n)), \\ t_{n+1} &= t_n + \Delta t_n, \end{aligned}$$

where $K$ and $M$ are *static* and depending on $\mathcal{H}^{-1}$, $F$ and $\Delta t_n$.

In many cases however, the $t$-local numerical resolution of (7) would be too complex or expensive: the notion of *parametrizing* introduced in the sequel is devoted to such situations.

**Example 1** *For explicit dynamic models, any question relating to the uniqueness of $x$ (for example initial conditions) must be taken into account in the definition of $\mathcal{H}$ and $F$. Consider for example a differential system in a Banach state space* $\mathbf{E}$*:*

$$\left\{ \begin{array}{l} \partial_t x = f(v, x) \\ x(0) = x_0; \end{array} \right.$$

*by denoting $u := (v, x_0)^T$, we get:*

$$\mathcal{H}x = (\partial_t x, x(0))^T, \;\; F(u, x) = (f(v, x), x_0)^T,$$

*with (for example): $\mathcal{X} \subset C^1(\mathbb{R}_t^+; \mathbf{E})$, $\mathcal{U} \subset \mathcal{V} \times \mathbf{E}$, $\mathcal{E} = C^0(\mathbb{R}_t^+; \mathbf{E}) \times \mathbf{E}$. Note that this formulation is generic: beyond controls*[5]*, $v$ can include physical parameters to be identified, an estimation $\hat{g}$ of a quantity $g(x)$ from measures, etc.*

**Example 2** *Volterra models, where $\mathcal{H} = H(\partial_t)$ [4], with $\mathcal{X} \subset C^1_+(\mathbb{R}_t; \mathbf{E}) = \{x \in C^1(\mathbb{R}_t; \mathbf{E}),\ \mathrm{supp}\, x \subset \mathbb{R}^+\}$ and $\mathcal{U} \subset L^1_+(\mathbb{R}_t; \mathbf{E})$.*

## 4 Model parametrizing: abstract definitions and properties

In some papers relating to linear model parametrizing (cf. for example [15], [13]), the considered parametrizing is explicitly expressed (cf. definition 2). We introduce here the more flexible notion of *parametric equation* (cf. definition 3), the solution of which is a parametrizing. If the resolution of such an equation is cheaper or is more robust than the resolution of the model, it will be advantageous to consider it to simplify problems like (8).

Moreover, a parametric equation formally appears as a new model (cf. definition 4) equivalent *or not* (in the sense it has less solutions) to the initial model (7), following the own properties of the parametric equation.

In the sequel, we denote $\mathcal{Z} := \mathcal{U} \times \mathcal{X}$ and $z := (u, x)$ (NB: extensions to more general situations can be obtained *mutatis mutandis* with $z := \mathbf{G}(u, x)$, $\mathbf{G} \in \mathrm{Isom}(\mathcal{U} \times \mathcal{X}; \mathcal{Z})$).

**Definition 2** *A parametrizing of (7) is defined by a topological space $\mathcal{Y}$ and a continuous application $\mathbf{Q} : \mathcal{Y} \to \mathcal{Z}$ such that $\forall y \in \mathcal{Y}$, $\mathbf{Q}(y)$ is solution of (7).The argument $y$ of $\mathbf{Q}$ is called the parameter.*

Note that $(I_{\mathcal{Z}}, \mathrm{graph}(\mathbf{F}))$ is always a (trivial) parametrizing (the parameter is $y = z$).

From a formal point of view, $(\mathbf{Q}, \mathcal{Y})$ is a parametrizing of the equations $\Phi = 0$ if and only if $\Phi \circ \mathbf{Q} = 0$ (as an application $\mathcal{Y} \to \mathcal{E}$):

$$\mathcal{Y} \xrightarrow{\mathbf{Q}} \mathcal{Z} \xrightarrow{\Phi} \mathcal{E} \Leftrightarrow \mathcal{Y} \xrightarrow{\mathbf{Q}} \mathcal{Z} \xrightarrow{\Phi} \mathcal{E} \to 0.$$

Let $\mathcal{F}$ a topological vector space and $\Psi : \mathcal{Z} \times \mathcal{Y} \to \mathcal{F}$ an application.

**Definition 3** *The equation in $\mathcal{Z} \times \mathcal{Y}$:*

$$\Psi(z, y) = 0 \tag{9}$$

*is a parametric equation for (7) if there exists a parametrizing $(\mathbf{Q}, \mathcal{Y})$ of (7) such that $\Psi(z, y) = 0 \Leftrightarrow z = \mathbf{Q}(y)$.*

In other words, $\Psi(z, y) = 0 \Rightarrow \Phi(z) = 0$ (that is $z$ is a solution of (7)): solving the parametric equation $\Psi(z, y) = 0$ consists in expressing all or some solutions $(u, x)$ of (7) from a (same) parameter $y \in \mathcal{Y}$. Furthermore, $\mathbf{Q}' := (\mathbf{Q}, I)$ is a parameter of the "model" (9) and we have the equivalences

$$\begin{array}{rcl} \mathcal{Y} \xrightarrow{\mathbf{Q}} \mathcal{Z} \xrightarrow{\Phi} \mathcal{E} & \Leftrightarrow & \mathcal{Y} \xrightarrow{\mathbf{Q}} \mathcal{Z} \xrightarrow{\Phi} \mathcal{E} \to 0 \Leftrightarrow \\ \mathcal{Y} \xrightarrow{\mathbf{Q}'} \mathcal{Z} \times \mathcal{Y} \xrightarrow{\Psi} \mathcal{F} & \to & 0 \Leftrightarrow \mathcal{Y} \xrightarrow{\mathbf{Q}'} \mathcal{Z} \times \mathcal{Y} \xrightarrow{\Psi} \mathcal{F}. \end{array}$$

It can be shown:

**Proposition 1** *A parametric equation $\Psi(z, y) = 0$ is a well-posed problem in $y$.*

Thus, $\Psi(z, y) = 0$ is a new model (of state $z$ and data $y$). Using this parametrizing, the problem (8) is transformed into:

$$\min\{J(z);\ (z, y) \in \mathcal{Z} \times \mathcal{Y},\ \Psi(z, y) = 0\}. \tag{10}$$

We have: $z = \mathbf{Q}(y) \Rightarrow x = \mathbf{F}(u)$; thus:

$$\begin{array}{ll} \Psi(z, y) = 0 & \text{(parametric model)} \\ \Downarrow & \\ \Phi(u, x) = 0 & \text{(state model).} \end{array}$$

[5] For example in $L^\infty(\mathbb{R}_t^+; \mathbb{R}^m)$.

Even if (10) can seem to be more complex (especially because $(z, y) = (u, x, y)$), this parametrized problem may be simpler than the initial one. In particular (but not only in this case), if $\mathbf{Q} = (\mathbf{B}, \mathbf{C})$ can be explicitly written by means of known operators (cf. for example § 5 and [14]), then $(u, x) = (\mathbf{B}(y), \mathbf{C}(y))$ is solution of (7) for any $y \in \mathcal{Y}$. We deduce that (10) can be reduced as:

$$\min\{\tilde{J}(y);\ y \in \mathcal{Y}\}, \tag{11}$$

with $J(y) := J(\mathbf{Q}(y), y)$.

**Remark 2** *Note that, due to the definition of parametrizing, the problems (8) and (10) are not necessarily equivalent, in particular if* $\mathrm{Im}(\mathbf{Q}) \subsetneq \mathrm{graph}(\mathbf{F})$ *(i.e.* $\mathbf{B}$ *is not surjective).*

In the parametrizing approach, the main problem is to establish from a given model a suitable parametrizing or, when this is not possible, a suitable parametric equation. The practical interest will be effective when (9) can be solved robustly and cheaply while (7) cannot. When such a goal is reached, the parametric model can legitimately be viewed as the "good" one.

Finally, various other properties of $\mathbf{Q}$ can be searched, according to the features of the problem under consideration. We can define in particular:

**Definition 4** *A parametrizing* $(\mathbf{Q}, \mathcal{Y})$ *is said complete if* $\mathbf{Q}$ *is an homeomorphism between* $\mathcal{Y}$ *and* $\mathrm{graph}(\mathbf{F})$*, and a parametric equation is said complete when its solution is a complete parametrizing.*

**Remark 3** *Although complete parametrizing or parametric equation associated with a given model often appears more natural, namely for control problems, the property of invertibility of* $\mathbf{Q}$ *is not possible in many situations. Nevertheless, the notion of (non invertible) parametrizing remains useful in such cases.*

In the example studied in the next section, many of the notions introduced above are involved. More details and various results relating to parametrizing will be given in a further publication.

# 5 Application of operatorial parametrizing to fed-batch bioreactor control problems

Fermentation is a critical process of production of substances from organic molecules. The high cost associated to many fermentation processes makes optimization of bioreactor performance very desirable. Unfortunately, the bioreactor dynamic models are highly nonlinear, which makes optimal control a difficult problem studied in many works [8], [7], [12],[5] and with many industrial applications (maximization of bioethanol production etc.).

We show in the sequel how operatorial parametrizing significantly simplifies control problems relating to fed-batch bioraector equations.

## 5.1 The model under consideration

We consider the following model of fed-batch bioreactors [11]:

$$\begin{cases} \partial_t x = \mu(X)\, x - x\, u \\ \partial_t s = -a_1 \mu(X)\, x + (s_i - s)\, u \\ \partial_t p = a_2 \mu(X)\, x - p\, u \\ X(0) = X_0, \end{cases} \tag{12}$$

where $x, s, p$ are the respective concentrations of biomass, substrate and product, $X = (x, s, p)^T$, $\mu$ is the growth rate, $s_i$ the substrate concentration in feed, $u$ (the control) is the dilution of feed and $X_0$ the initial conditions.

## 5.2 Operatorial parametrizing of (12)

### 5.2.1 Time-scale transformation

We consider the time-scale transformation $z \mapsto \widetilde{z} := z \circ \varphi^{-1}$, with $\varphi : t \mapsto \tau$ such that $\varphi' = u > 0$ and $\varphi(0) = 0$, that is[6]:

$$\varphi = \partial_t^{-1} u. \tag{13}$$

The associated TST has the following expression:

$$S : (u, z) \mapsto \widetilde{z} = z \circ \left(\partial_t^{-1} u\right)^{-1},$$

where $\widetilde{z}$ denotes the trajectory $z$ in time $\tau = \varphi(t)$.
For convenience, we will denote:

$$S_u := S(u, \cdot).$$

**Remark 4** *In the same way, we denote*

$$\widetilde{u} := S_u(u) = u \circ \left(\partial_t^{-1} u\right)^{-1}.$$

Then, we know that:

$$S_u^{-1} : \widetilde{z} \mapsto z = \widetilde{z} \circ \left(\partial_t^{-1} u\right).$$

Moreover, as $d\tau = u\, dt$, we have:

$$\left(\varphi^{-1}\right)' = \frac{1}{\widetilde{u}}$$

and then:

$$\varphi^{-1} = \partial_\tau^{-1} \frac{1}{\widetilde{u}},$$

[6] We denote $\partial_t^{-1}$ the operator $u \mapsto \int_0^t u\, ds$

from which we deduce different expressions of operators $z \mapsto \widetilde{z}$ and $\widetilde{z} \mapsto z$ :

$$S_{\frac{1}{\widetilde{u}}}^{-1} : z \mapsto \widetilde{z} = z \circ \partial_\tau^{-1} \tfrac{1}{\widetilde{u}}$$
$$S_{\frac{1}{\widetilde{u}}} : \widetilde{z} \mapsto z = \widetilde{z} \circ \left(\partial_\tau^{-1} \tfrac{1}{\widetilde{u}}\right)^{-1}.$$

By denoting $T_{\tilde{u}} := S_{\frac{1}{\widetilde{u}}}^{-1}$, we then have two expressions of the time-scaling transformation (and its inverse) depending respectively on $u$ and $\tilde{u}$, as summerized in the following scheme:

$$z \underset{S_u^{-1}, T_{\tilde{u}}^{-1}}{\overset{S_u, T_{\tilde{u}}}{\longrightarrow \atop \longleftarrow}} \widetilde{z}.$$

As $\partial_t \varphi = u$, we can remark that the proposed time-scale transformation is governed by the feed dilution of the bioreactor, which is rather natural. Moreover, it is causal and then can be used in real time applications.

We will denote by $\mathbf{S}$ the operator $z \mapsto \widetilde{z}$, indifferently referring to its expression depending on $u$ (that is $S_u$) or $\widetilde{u}$ (that is $T_{\tilde{u}}$). For simplicity of notations, we consider that $\mathbf{S}$ can be applied either to scalar or vectorial trajectories by using the convention:

$$\mathbf{S}(z_1, ..., z_n) := (\mathbf{S}(z_1), ..., \mathbf{S}(z_n)).$$

#### 5.2.2 Parametrizing operators

Consider now the following operator:

$$\begin{aligned} \mathbf{A} : \quad & C^\infty(\mathbb{R}_t^+; \mathbb{R}) \times C^\infty(\mathbb{R}_t^+; \mathbb{R}^3) \to C^\infty(\mathbb{R}_t^+; \mathbb{R}) \times \mathbb{R}^3 \\ & (u, X) \mapsto y = (\widetilde{\mathbf{A}} \circ \mathbf{S})(u, X) \end{aligned}$$

where

$$\begin{aligned} \widetilde{\mathbf{A}} : \quad & C^\infty(\mathbb{R}_\tau^+) \times C^\infty(\mathbb{R}_\tau^+; \mathbb{R}^3) \to C^\infty(\mathbb{R}_\tau^+; \mathbb{R}) \times \mathbb{R}^3 \\ & (\widetilde{u}, \widetilde{X}) \mapsto \left( \tfrac{\mu(\widetilde{X})\widetilde{x}}{\widetilde{u}}, \langle \delta, \widetilde{x} \rangle, \langle \delta, \widetilde{s} \rangle, \langle \delta, \widetilde{p} \rangle \right)^T \end{aligned}$$

Note that the terms $\langle \delta, \widetilde{x} \rangle$ relate to initial conditions of (12).

By applying the operator $\mathbf{S}$ on (12), simple computations, based on $y = \mathbf{A}(u, X)$ and the property $\frac{dx}{dt} = \frac{dx}{d\tau}\frac{d\tau}{dt}$, lead to the following linear system:

$$\begin{cases} \partial_\tau \widetilde{x} = -\widetilde{x} + y_1 \\ \partial_\tau \widetilde{s} = -\widetilde{s} + s_i - a_1 y_1 \\ \partial_\tau \widetilde{p} = -\widetilde{p} + a_2 y_1, \end{cases} \tag{14}$$

where $y_i$, $i = 1:4$ denotes the ith component of $y$. Furthermore, we deduce from (14) the expression of the associated operators $(\mathbf{B}, \mathbf{C})$:

$$\begin{aligned} u &= \mathbf{B}(y) = (\mathbf{S}^{-1} \circ \widetilde{\mathbf{B}})(y) \\ X &= \mathbf{C}(y) = (\mathbf{S}^{-1} \circ \widetilde{\mathbf{C}})(y), \end{aligned} \tag{15}$$

with:

$$\widetilde{\mathbf{C}}(y) = \begin{pmatrix} (\partial_\tau + 1)^{-1}(y_1) + y_2\, e^{-(\cdot)} \\ (\partial_\tau + 1)^{-1}(s_i - a_1\, y_1) + y_3\, e^{-(\cdot)} \\ (\partial_\tau + 1)^{-1}(a_2\, y_1) + y_4\, e^{-(\cdot)} \end{pmatrix}$$

$$\widetilde{\mathbf{B}}(y) = \tfrac{\mu(\mathbf{C}(y))\, \mathbf{C}_1(y)}{y_1}.$$

We can remark that those operators are finite combination of static/linear dynamic/TST operators. Up to the above operatorial transformations, the system (14) is equivalent to (12).

Then, classical control methods of linear systems can be investigated on (14) (optimal control, linear feedback stabilization, predictive control and so on), and straightforward solutions relating to (12) are directly deduced from the ones of (14) by means of (15).

Figures 1,2,3 highlight how such solutions can be implemented on the physical process.

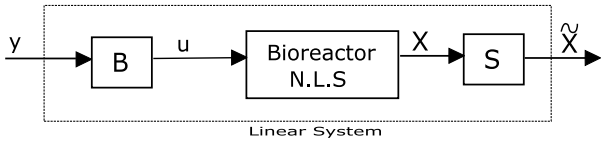


**Figure 1. The linear system (14)**

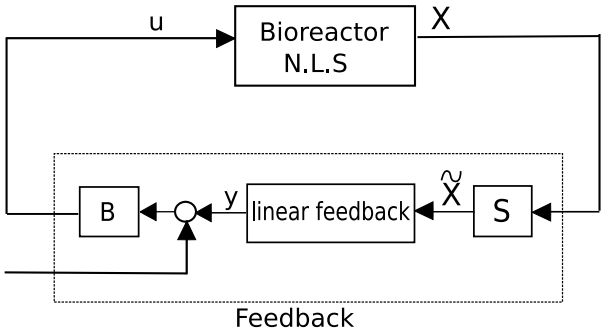


**Figure 2. Stabilizing feedback control**

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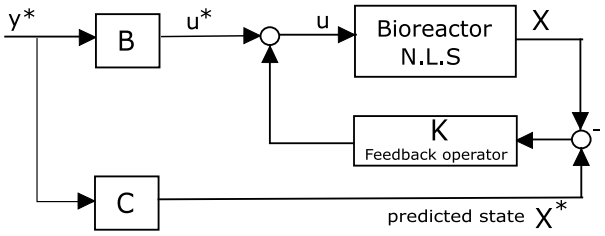


**Figure 3. Predictive control**


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