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# CONTROLLING NONLINEAR INFINITE-DIMENSIONAL SYSTEMS VIA THE INITIAL STATE

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Abstract. A control problem is considered for nonlinear time-varying systems described by partial differential equations, in which the control acts only via part of the initial state. The problem is to drive part, or all, of the process to some desired state in a specified time. The motivation for such systems are control problems arising in medicine and biology that involve spatial or age characteristics, or time-delays. The approach taken is to formulate the problem as a fixed point problem for a suitable abstract differential equation and then apply a version of the Contraction Mapping Theorem. Conditions are imposed so that the problem is well defined and a weaker form of solution exists. The solution obtained ensures that the target state is achieved on the range of a linear operator arising from a linearisation of the system about an initial estimate for the control. Although the Contraction Mapping Theorem yields a constructive method to determine the solution an alternative, more direct, approach is presented, which relies on an iterative scheme for the control and the original dynamics.

Key words. distributed parameter systems, initial state control, fixed point theorems

AMS subject classifications. 93C10, 93C20, 93C25

1. Introduction. The control problem which this paper considers is to drive some part (or all) of a particular process to some desired state in a specified time, when the control acts only via the initial state. For example, in [7] the problem of controlling the spread of rabies in a fox population was considered where the initial distribution of vaccinated and/or culled foxes had to be chosen such that the combined distribution of infected foxes was some desired target. In this case the parts of the system that were controlled were the population densities of incubating and rabid foxes, while the control represented the distribution of vaccinated and/or culled foxes produced via a suitable intervention. In [7] the control problem was formulated in terms of an abstract differential equation with the part of the state to be controlled as an output. Thus the problem became that of driving the output of the system to a desired value in a specified time using only an input term in the initial condition.

This paper addresses the problem in [7] in a more general setting that permits unboundedness of the nonlinearity and proposes an alternative, iterative scheme for determining the required control. In addition, the control problem is generalised slightly by permitting multiple impulsive inputs. The mathematical formulation of the control problem is as follows: Consider the system of differential equations on a Banach space Z given by the following

$$\dot{\overline{z}}_i(t) = f(t, \overline{z}_i(t)), \qquad \overline{z}_i(\tau_i) = \overline{z}_{i-1}(\tau_i) + B\overline{u}_i, i = 1, \dots, m,$$

where f is nonlinear, the m inputs,  $\overline{u}_1, \ldots, \overline{u}_m$ , are applied at times  $0 = \tau_1 < \tau_2 < \cdots < \tau_m$ , and  $\overline{z}_0(0) = \overline{z}_0$  denotes the known, given initial state of the equation without input. The linear operator B determines how the control acts via the given state. he states from these systems of equations can be pieced together to form the trajectory  $\overline{z}(t) = \overline{z}_i(t)$ , for  $t \in [\tau_i, \tau_{i+1})$ ,  $i = 1, \ldots, m$ , where  $\tau_{m+1} = T$  for some fixed time T.

The controls,  $\overline{u}_i$ , are assumed to belong to the same Hilbert space U such that  $B \in \mathcal{L}(U, Z)$ . Therefore the treatment of this paper is confined to the situation

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involving bounded inputs. If, for the underlying system, it is not possible to affect the state at every point of the spatial domain so that the controls are restricted to only a few points or parts of the boundary the resulting model will involve an *unbounded* input operator. Following the approach of [16] for systems with unbounded inputs and outputs, it can be assumed that there exists a Banach space  $Z \subset Z_1$  with continuous injection and dense range. The input operator is then assumed to be bounded from U to  $Z_1$ .

The output associated with the differential equation is given by

$$y = C\overline{z}_m(T),$$

where T is the specified time and the output takes values in a Hilbert space Y. The control problem is to choose the  $\overline{u}_i$  such that the resulting output is  $y = y_d$ , the desired target output.

Suppose that initial guesses are made for the control,  $\hat{u}_i$  say, with associated differential equations

$$\dot{\hat{z}}_i(t) = f(t, \hat{z}_i(t)), \qquad \hat{z}_i(\tau_i) = \hat{z}_{i-1}(\tau_i) + B\hat{u},$$
 (1.1)

where  $\hat{z}_0(0) = \overline{z}_0$  and that these equations have continuously differentiable solutions  $\hat{z}_i(\cdot)$ . While this control might be a good initial guess there is no reason to assume that the output of this system,  $C\hat{z}_m(T)$ , is the desired final state. Therefore a local approximation is made by setting  $\overline{z}_i = \hat{z}_i + z_i$  and  $\overline{u}_i = \hat{u}_i + u_i$  to get

$$\dot{z}_i(t) + \dot{z}_i(t) = f(t, z_i(t) + \hat{z}_i(t)), \qquad z_i(\tau_i) = z_{i-1}(\tau_i) + Bu_i, \tag{1.2}$$

for  $i=1,\ldots,m$ , where  $z_0(0)=0$ . Now suppose that f is differentiable around the trajectory  $\{(t,z'(t)):t\in[0,T]\}$  in the sense that

$$f(t,\overline{z}_i) = f(t,\hat{z}_i(t)) + A(t)\left(\overline{z}_i - \hat{z}_i(t)\right) + N(t,(\overline{z}_i - \hat{z}(t))) \tag{1.3}$$

for some piecewise continuous  $A(\cdot)$  such that A(t) is an unbounded linear operator on Z for each  $t \in [0,T]$ . In the following, to permit unboundedness of the nonlinearity on Z, it will be assumed that there are Banach spaces  $\underline{Z}$  and  $\overline{Z}$  such that that  $N:[0,T]\times \underline{Z}\longrightarrow \overline{Z}$ . More precise assumptions will be introduced in the following section.

Equation (1.2) therefore can be rewritten as

$$\dot{z}_i(t) = A(t)z_i(t) + N(t, z_i(t)), \qquad z_i(\tau_i) = z_{i-1}(\tau_i) + Bu_i,$$
 (1.4)

for i = 1, ..., m, where  $z_0(0) = 0$ .

In §3 the first stage of the control problem is considered, namely the construction of inputs that give rise to a mild solution with the desired properties. A fixed point theorem is applied to give the solution using the following version of the Contraction Mapping Theorem from [2]:

Theorem 1. Suppose that  $\varphi:W\longrightarrow W$  is a mapping between Banach spaces that satisfies

$$\|\varphi x - \varphi y\| \le k\|x - y\|, \quad 0 \le k < 1$$

(k a constant), for  $x, y \in D$ , a subset of W. If both the ball

$$S = \left\{ w \in W : \|w - w_1\| \le \frac{k}{1 - k} \|w_1 - w_0\| \right\}$$

and  $w_0$  lie in D, then the iterative process  $w_{i+1} = \varphi w_i$  converges to a unique fixed-point in D.

The earliest use of fixed point methods in a control context was in [8] for finite-dimensional systems. In [4] the application of fixed point methods to finite-dimensional time-varying systems was presented, and this approach has been extended to infinite-dimensional systems in [11]. An early review of the use of fixed point methods in nonlinear control and observation is provided in [1].

In §2 the general framework for considering the control problem is proposed and the control problem itself is solved in §3 using a fixed point approach. An equivalent, but less intuitive, method for constructing the control is given in §4. This method exploits the original system dynamics and uses an adaptive scheme to give the solution. This method readily lends itself to numerical simulation and constructs the control directly rather than via a mild solution (as is the case in the fixed point approach). Motivated by the example in [7] a class of systems is considered in §5 in which the linear part of the dynamics arises from a time-varying perturbation of the (time-invariant) generator of a strongly continuous semigroup. In contrast with [7] the perturbation is permitted to exhibit unboundedness comparable with that of the nonlinearity. Finally to illustrate the application of the approach proposed in this paper a case study is considered in §6, in which the problem of determining a dosing schedule to control the viral load in a HIV patient is solved. The solution exploits the iterative approach of §4 applied to the numerical solution of the system delaydifferential equations. This case study illustrates how even the single input version (m=1) of the theory can be applied to yield results for multiple inputs. For the case study this is achieved because the inputs affect states that appear linearly in the model so that the system can be formulated in terms of a delay differential system.

## 2. Mathematical framework. In this section the general system given by

$$\dot{z}_i(t) = A(t)z_i(t) + N(t, z_i(t)), \qquad z_i(\tau_i) = z_{i-1}(\tau_i) + Bu_i,$$
 (2.1)

is considered in order to provide an abstract framework in which to tackle the control problem. Consider for the moment the linear part of (2.1), with arbitrary initial state, given by

$$\dot{z}_i(t) = A(t)z_i(t), \qquad z_i(s) = z_s,$$
 (2.2)

with  $s \in [0, T]$ . In the time-invariant case, if A is a densely defined linear operator on Z with non-empty resolvent set  $\rho(A)$ , then it is well known that the Cauchy problem (2.2) is well-posed if and only if A is the generator of a strongly continuous semigroup [15]. In the time-varying case the situation where A(t) is the generator of a strongly continuous semigroup for each  $t \in [0, T]$  was considered in [17] and that when A(t) is strongly continuous with domain independent of t in [10]. Adopting the setting in [9], who weakened the latter assumption, the following assumption is made:

Assumption 1. A(t) is a linear operator on Z for all  $t \in [0,T]$  with domain D(A), which is independent of t and dense in Z. For all  $z \in D(A)$  the map  $t \mapsto A(t)z$  is continuous except on a finite set of discrete points J. For each  $\tau \in J$  and  $z \in D(A)$  the one-sided limits  $\lim_{t \downarrow \tau} A(t)z$ ,  $\lim_{t \uparrow \tau} A(t)z$  exist.

By allowing A(t) to be only piecewise continuous Hinrichsen and Pritchard [9] were able to slightly weaken the definition appearing in the literature for the time-varying Cauchy problem given by (2.2) to be well-posed. In parallel with the time invariant case the Cauchy problem (2.2) is well-posed if and only if there is a strong evolution operator  $(U(t,s))_{(t,s)\in\Delta(T)}$  with generator  $A(\cdot)$  [9].

For the full problem (2.1), even in the time-invariant case with bounded non-linearity, in general it cannot be guaranteed that the resulting Cauchy problem is well-posed. However, if  $N(\cdot, z(\cdot)) \in PC(s, T; Z)$  and the Cauchy problem is well-posed with solution  $z(\cdot)$ , and strong evolution operator U(t, s), then

$$z(t) = U(t, s)z_s + \int_s^t U(t, \sigma)N(\sigma, z(\sigma)) d\sigma.$$

Therefore, in the following, the control problem will first be considered with respect to the corresponding mild solutions:

$$z_{i}(t) = U(t, \tau_{i}) \left( z_{i-1}(\tau_{i}) + Bu_{i} \right) + \int_{\tau_{i}}^{t} U(t, s) N(s, z_{i}(s)) \, \mathrm{d}s, \tag{2.3}$$

for i = 1, ..., m, where  $z_0(0) = 0$  and  $u_i \in U$ , a Hilbert space such that  $B \in \mathcal{L}(U, Z)$  and U(t, s) is a mild evolution operator on Z. Suppose that the following assumptions hold:

TV 1.  $\underline{Z} \subset \overline{Z}$  are Banach spaces such that the nonlinearity  $N: [0,T] \times \underline{Z} \longrightarrow \overline{Z}$  maps functions in  $L^p(0,T;\underline{Z})$  to functions in  $L^q(0,T;\overline{Z})$  for real numbers  $p,q \geq 1$  in the sense that

$$(\mathcal{N}z)(\cdot) = N(\cdot, z(\cdot)) \in L^q(0, T; \overline{Z}) \quad whenever \quad z(\cdot) \in L^p(0, T; Z).$$

TV 2. U(t,s) is a mild evolution operator on all three spaces  $\underline{Z}$ , Z and  $\overline{Z}$ . TV 3. There exists a  $k_1(\cdot) \in L^r(0,T)$ , with  $\frac{1}{r} + \frac{1}{q} = \frac{1}{p} + 1$ , such that for all

(t, s)  $\in \Delta(T)$ ,  $U(t, s) \in \mathcal{L}(\overline{Z}, \underline{Z})$  and

$$||U(t,s)z||_Z \le k_1(t-s)||z||_{\overline{Z}} \quad \text{for all } z \in \overline{Z}.$$
 (2.4)

Let  $K_1 = ||k_1(\cdot)||_{L^r(0,T)}$ .

TV 4. There exists a  $k_2(\cdot) \in L^p(0,T)$  such that for all  $(t,s) \in \Delta(T)$  and  $u \in U$ ,  $U(t,s)Bu \in \underline{Z}$  and

$$||U(t,s)Bu||_{Z} \le k_{2}(t-s)||u||_{U}. \tag{2.5}$$

Let  $K_2 = ||k_2(\cdot)||_{L^p(0,T)}$ .

The above assumptions ensure that the following operator is well-defined (in  $\underline{Z}$ )

$$\left(\mathbb{M}_{U}h\right)(t) = \int_{0}^{t} U(t,s)h(s) \,\mathrm{d}s \qquad \text{for all } h(\cdot) \in L^{q}(0,T;\overline{Z}). \tag{2.6}$$

Moreover, the map  $t \mapsto (\mathbb{M}_U h)(t)$  is continuous with respect to  $\|\cdot\|_{\underline{Z}}$  and the following notion of weak solution is well defined for (2.3):

DEFINITION 1. A mild solution of (2.3) is any piecewise-continuous function  $z(\cdot) \in PC(0,T;Z)$  (with discontinuities at  $t = \tau_i$ ) such that  $z(t) \in \underline{Z}$  for almost all  $t \in [0,T]$ ,  $z(\cdot)$  is  $L^p$ -integrable in  $\underline{Z}$  on every interval [0,t] and (2.3) is satisfied for all  $t \in [0,T]$ .

Therefore a mild solution,  $z(\cdot)$ , of (2.3) is sought such that the output given by

$$y = C\hat{z}(T) + Cz(T) = C\hat{z}_m(T) + Cz_m(T),$$
 (2.7)

where  $y \in Y$  for a suitable Hilbert space Y, is some specified value  $y_d$ . For considerations to be discussed in greater detail later, it is necessary to assume that the range of  $\phi$  is a closed subspace of Y, and therefore it might not be possible to consider C as a bounded linear operator from Z to Y. Therefore, the following assumption is made:

TV 5. There exists a Banach space  $V \subset Z$ , with continuous injection, such that  $C \in \mathcal{L}(V,Y)$ . In addition, for all k = 1, ..., m and  $u \in U$ ,  $U(T, \tau_k)Bu \in V$ , with constant  $K_3$  such that

$$||U(T,\tau_k)Bu||_V \le K_3||u||_U.$$

There exists a constant  $K_4$  such that  $(\mathbb{M}_U h)(T) \in V$  and

$$\| (\mathbb{M}_{U}h)(T) \|_{V} \leq K_{4} \| h \|_{L_{q}(0,T;\overline{Z})}$$

for all  $h \in L^q(0,T;\overline{Z})$ .

**3.** The control problem. Considering for the moment only the linear dynamics, the control problem is to find  $\tilde{u}_i$  (i = 1, ..., m) such that the output

$$y = C\hat{z}(T) + CU(T, \tau_m) (B\tilde{u}_m + z_{m-1}(\tau_m))$$
$$= C\hat{z}(T) + \sum_{k=1}^m \phi_k \tilde{u}_k \quad \text{where } \phi_k = CU(T, \tau_k)B,$$

is the desired value  $y_d$ . For the Hilbert space  $\mathcal{U} = U^m$  with inner product  $\langle u, v \rangle_{\mathcal{U}} = \sum_{k=1}^m \langle u_k, v_k \rangle_U$ , let  $\Phi : \mathcal{U} \longrightarrow Y$  be the linear map defined by  $\Phi(\tilde{u}_1, \dots, \tilde{u}_m) = \sum_{k=1}^m \phi_k \tilde{u}_k$ . If  $y_d - C\hat{z}(T) \in \operatorname{ran} \Phi$  then a solution exists. In particular, if  $\Phi$  is invertible, then there is a unique solution given by

$$\tilde{u} = (\tilde{u}_1, \dots, \tilde{u}_m) = \Phi^{-1} (y_d - C\hat{z}(T)).$$

Therefore the linear part of the system can be steered to  $\{y \in Y : y - C\hat{z}(T) \in \operatorname{ran} \Phi\}$ . In the literature [12, 1] it is usual to consider the nonlinear problem on this subspace, with some suitable topology defined on it:

LEMMA 1. The range of  $\Phi$  is a Banach space  $R(\Phi)$ , with a suitably defined norm. Proof. Since  $\Phi$  is a bounded linear operator, define the space X by

$$X := \mathcal{U}/\ker \Phi$$
.

Since  $\ker \Phi$  is closed X is a Banach space under the norm

$$||[u]||_X = \inf_{u \in [u]} ||u||_{\mathcal{U}} = \inf_{\Phi \tilde{u} = 0} ||u + \tilde{u}||_{\mathcal{U}}.$$

Now define  $\tilde{\Phi}: X \longrightarrow Y$  by

$$\tilde{\Phi}[u] = \Phi \tilde{u} \qquad \tilde{u} \in [u].$$

Then  $\tilde{\Phi}$  is injective and

$$\|\tilde{\Phi}[u]\|_{Y} \le \|\Phi\| \|[u]\|_{X}.$$

Now define a norm on the range of  $\tilde{\Phi}$  by

$$||v||_{R(\Phi)} := ||\tilde{\Phi}^{-1}v||_X.$$

This norm is equivalent to the graph norm on  $D(\tilde{\Phi}^{-1})$ . Since  $\tilde{\Phi}$  is bounded and  $D(\tilde{\Phi})(=X)$  is closed it holds that  $\tilde{\Phi}$  is a closed linear operator and so  $\tilde{\Phi}^{-1}$  is also closed [18]. Therefore it follows that  $R(\Phi)$  is a Banach space with the above norm.  $\square$ 

For any  $y_d \in Y$  such that  $y_d - C\hat{z}(T) \in R(\Phi)$ , since  $\mathcal{U}$  is a Hilbert space and  $\ker \Phi$  is closed the infimum in the definition of  $\|\cdot\|_X$  is attained and so there is a  $u \in \mathcal{U}$  such that  $u = \tilde{\Phi}^{-1}(y_d - C\hat{z}(T))$  that minimises  $\|u\|_{\mathcal{U}}$  over all controls that achieve  $y = y_d$ . Thus a more general form of the linear problem is to find a least squares solution that minimises

$$||[y_d - C\hat{z}(T)] - \Phi u||_Y$$
 (3.1)

over all choices of  $u \in \mathcal{U}$ , and with the smallest norm in  $\mathcal{U}$ . This control, provided  $y_d - C\hat{z}(T) \in \operatorname{ran} \Phi + (\operatorname{ran} \Phi)^{\perp}$ , is given by [14]

$$\tilde{u} = \Phi^{\dagger} \left( y_d - C\hat{z}(T) \right)$$

where  $\Phi^{\dagger}$  is the generalised inverse of  $\Phi$ .

For the nonlinear problem this suggests that the control given by

$$\tilde{u} = \Phi^{\dagger} \left( y_d - C\hat{z}(T) - C \int_0^T U(T, s) N(s, z(s)) \,\mathrm{d}s \right)$$
(3.2)

be applied. However this is an implicit expression since the state  $z(\cdot)$  is dependent on the control. If a solution exists then the output is driven to the following

$$y = \Phi \Phi^{\dagger} y_d + \left( I - \Phi \Phi^{\dagger} \right) \left[ C \hat{z}(T) + C \int_0^T U(T, s) N(s, z(s)) \, \mathrm{d}s \right]. \tag{3.3}$$

If  $\Phi$  is invertible then  $\Phi^{\dagger} = \Phi^{-1}$  and (3.3) reduces to  $y = y_d$ . If  $\Phi$  is not invertible, but  $y_d - C\hat{z}(T) \in \operatorname{ran} \Phi$ , then (3.3) reduces to the following:

$$y = y_d + (I - \Phi \Phi^{\dagger}) \left[ C \int_0^T U(T, s) N(s, z(s)) ds \right].$$

REMARK 1. The first term of (3.3), in the case where the range of  $\Phi$  is closed, is the orthogonal projection of  $y_d$  onto ran  $\Phi$  and the second is the orthogonal projection onto ran  $\Phi^{\perp}$ . Therefore, on the range of  $\Phi$ , the control drives the system to the desired final state.

For notational convenience denote by  $\tilde{U}(t,s)$  the family of bounded linear operators defined as follows:

$$\tilde{U}(t,s)z = \begin{cases} U(t,s)z & t \ge s \\ 0 & t < s \end{cases}$$

for  $z \in Z$ . Therefore the controllability problem is reduced to that of finding a fixed point of the following map,  $\psi: L^p(0,T;\underline{Z}) \longrightarrow L^p(0,T;\underline{Z})$ :

$$(\psi z)(t) = \sum_{k=1}^{m} \tilde{U}(t, \tau_k) B \tilde{u}_k + (\mathbb{M}_U \mathcal{N} z)(t), \tag{3.4}$$

where  $\tilde{u} = \Phi^{\dagger} (y_d - C\hat{z}(T) - C(\mathbb{M}_U \mathcal{N}z)(T))$ . Once a fixed point has been found this can be readily substituted into the right-hand side of (3.2) to find the control. The

following result from [14] is important for the main theorem of this paper because it characterises when the generalised inverse of a bounded linear operator is itself bounded.

LEMMA 2. Let  $\Phi: U \longrightarrow Y$  be a bounded linear operator between two Hilbert spaces. Then the generalised inverse  $\Phi^{\dagger}$  is bounded if and only if the range of  $\Phi$  is a closed subspace of Y.

THEOREM 2. Consider the nonlinear system governed by

$$z(t) = \sum_{k=1}^{m} \tilde{U}(t, \tau_k) B u_k + \int_0^t U(t, s) N(s, z(s)) \, \mathrm{d}s,$$
 (3.5)

where U(t,s) is a mild evolution operator on Z, with output given by

$$y = Cz(T) + C\hat{z}(T) \tag{3.6}$$

for a given output  $C\hat{z}(T)$ . Suppose that the following conditions are satisfied:

- 1. Assumptions TV 1-5 hold.
- 2. The range of  $\phi$  is a closed subspace of Y.
- 3. The nonlinearity  $\mathcal{N}$  satisfies the following Lipschitz condition on the ball of radius a' about the origin,  $B_{a'}$ :

$$\|\mathcal{N}z - \mathcal{N}w\|_{L^{q}(0,T;\overline{Z})} \le k(\|z\|, \|w\|)\|z - w\|_{L^{p}(0,T;Z)}$$
(3.7)

for each  $z, w \in B_{a'}$  and some continuous symmetric function  $k(\cdot, \cdot) : \mathbb{R}^+ \times \mathbb{R}^+ \longrightarrow \mathbb{R}^+$  such that k(0,0) = 0.

4. Choose a < a' such that

$$\left(\sqrt{m}\,K_2\|\Phi^{\dagger}\|\,\|C\|K_4+K_1\right)\tilde{K}=K<1\tag{3.8}$$

where  $\tilde{K} = \sup_{0 \le \theta_1, \theta_2 \le a} k(\theta_1, \theta_2)$ .

Suppose that  $y_d \in Y$  satisfies

$$||y_d - C\hat{z}(T)||_Y \le \frac{a(1-K)}{\sqrt{m}K_2||\Phi^{\dagger}||}.$$
 (3.9)

Then there exists a control  $\tilde{u}$  of the form (3.2) that drives the output (3.6) to  $y_d$  on the range of  $\Phi$ .

*Proof.* The first step of the proof is to show that  $\psi$  is a contraction on  $B_a$ :

$$\|\psi z - \psi w\|_{L^{p}(0,T;\underline{Z})} \leq \sqrt{m} K_{2} \|\Phi^{\dagger} C\left(\mathbb{M}_{U}(\mathcal{N}w - \mathcal{N}z)\right)(T)\|_{\mathcal{U}}$$

$$+ \|\left(\mathbb{M}_{U}(\mathcal{N}z - \mathcal{N}w)\right)(\cdot)\|_{L^{p}(0,T;\underline{Z})}$$

$$\leq \left(\sqrt{m} K_{2} \|\Phi^{\dagger}\| \|C\|K_{4} + K_{1}\right) \tilde{K} \|z - w\|_{L^{p}(0,T;Z)}.$$

Therefore by (3.8)  $\psi$  is a contraction on  $B_a$ .

Since the initial guess for the control has been included in the initial state for  $\hat{z}$ , it seems natural to consider the iterative process given by  $z_n = \psi z_{n-1}$  with  $z_0 = 0$ . Then it is seen that

$$z_1(t) = \sum_{k=1}^{m} \tilde{U}(t, \tau_k) B u_k, \quad \text{where } u = \Phi^{\dagger} \left( y_d - C \hat{z}(T) \right).$$

Let  $S = \left\{ z \in L^p(0,T;\underline{Z}) : \|z - z_1\|_{L^p(0,T;\underline{Z})} \le \frac{K}{1-K} \|z_1\|_{L^p(0,T;\underline{Z})} \right\}$ . This will be contained in the ball of radius a if

$$\left(1 + \frac{K}{1 - K}\right) \left\| \sum_{k=1}^{m} \tilde{U}(\cdot, \tau_k) B u_k \right\|_{L^p(0, T; \underline{Z})} \le a,$$

which will be the case if

$$\frac{1}{1-K} \sqrt{m} \, K_2 \|\Phi^{\dagger}\| \, \|y_d - C\hat{z}(T)\|_Y \le a.$$

Rearranging this inequality yields (3.9) and so applying Theorem 1 proves the existence of a unique fixed point for  $\psi$ . Substituting this fixed point into (3.2) gives the control  $\tilde{u}$ .  $\square$ 

Note that the output resulting from applying the control given by the last theorem is only guaranteed to coincide with the desired state on the range of  $\phi$ . If there exists a control  $\tilde{u}$  such that the output, when applying this control, is the desired state, then it remains an open question whether the previous theorem gives the same control.

The proof of Theorem 2 provides an iterative scheme for obtaining the fixed point (and hence the control). In the next section a more direct method of finding the required control (and hence the fixed point) is given.

4. Iterative method for constructing control. The constructive method of the proof of Theorem 2 can be used to find the control that solves the control problem, but the desired control is found indirectly from the fixed point solution. In this section an alternative method for obtaining the control that gives rise to the solution of the fixed point problem is constructed. The method exploits the original dynamics and directly determines the required control without the need for further substitution.

The method used in this section is as follows: Consider the dynamical equations

$$z_n(t) = \sum_{k=1}^m \tilde{U}(t, \tau_k) Bu(n)_k + (\mathbb{M}_U \mathcal{N} z_n) (t)$$
(4.1)

where (as before) U(t,s) is a mild evolution operator on Z and the output is given by the following

$$y_n = Cz_n(T) + C\hat{z}(T). \tag{4.2}$$

The control u(n+1) is defined in terms of the previous control as follows

$$u(n+1) = u(n) + \Phi^{\dagger} (y_d - y_n).$$

For each  $n \in \mathbb{N}$  it must be shown that there exists a solution of the dynamical equation and that the iterative scheme for u(n) converges to the required solution of the fixed point problem.

Theorem 3. For each  $n \in \mathbb{N}$  consider the nonlinear system governed by

$$z_n(t) = \sum_{k=1}^m \tilde{U}(t, \tau_k) B u(n)_k + (\mathbb{M}_U \mathcal{N} z_n) (t).$$
 (4.3)

Suppose that the following conditions are satisfied:

1. Assumptions TV 1-5 hold.

- 2. The range of  $\phi$  is a closed subspace of Y.
- 3. The nonlinearity  $\mathcal{N}$  satisfies the following Lipschitz condition on the ball of radius a' about the origin,  $B_{a'}$ :

$$\|\mathcal{N}z - \mathcal{N}w\|_{L^{q}(0,T;\overline{Z})} \le k(\|z\|,\|w\|)\|z - w\|_{L^{p}(0,T;Z)} \tag{4.4}$$

for each  $z, w \in B_{a'}$  and some continuous symmetric function  $k(\cdot, \cdot) : \mathbb{R}^+ \times \mathbb{R}^+ \longrightarrow \mathbb{R}^+$  such that k(0, 0) = 0.

4. Choose  $a \leq a'$  such that

$$\left(\sqrt{m}\,K_2\|\Phi^{\dagger}\|\,\|C\|K_4+K_1\right)\tilde{K}=K<1\tag{4.5}$$

where  $\tilde{K} = \sup_{0 \le \theta_1, \theta_2 \le a} k(\theta_1, \theta_2)$ .

Suppose that  $y_d \in Y$  satisfies

$$||y_d - C\hat{z}(T)||_Y \le \frac{a(1-K)}{\sqrt{m} K_2 ||\Phi^{\dagger}||}.$$
 (4.6)

Then the iterative scheme u(0) = 0,

$$u(n) = u(n-1) + \Phi^{\dagger} (y_d - y_{n-1}) \qquad n \ge 1$$

gives rise to a mild solution  $z_n$  of (4.3) for each n and the sequence of controls, u(n), converges to the fixed point solution,  $\tilde{u}$ , of Theorem 2.

*Proof.* The theorem is proved in two steps: Firstly it is shown inductively that the scheme gives rise to a solution  $z_n$  for each  $n \in \mathbb{N}$ . Then it is shown that the scheme converges and that the limit is the fixed point solution from the previous section.

To show the existence of each solution,  $z_n$ , of (4.3) Theorem 1 will be applied to the operator  $\Psi: L^p(0,T;\underline{Z}) \longrightarrow L^p(0,T;\underline{Z})$  given by

$$(\Psi z_n)(t) = \sum_{k=1}^{m} \tilde{U}(t, \tau_k) Bu(n)_k + (\mathbb{M}_U \mathcal{N} z_n)(t). \tag{4.7}$$

Suppose that  $u(n) \in \mathcal{U}$  satisfies

$$||u(n)||_{\mathcal{U}} \le \frac{a\left(1 - K_1\tilde{K}\right)}{\sqrt{m}K_2}.\tag{4.8}$$

 $\Psi$  is a contraction on the ball  $B_a$  since, for  $z, w \in L^p(0,T;\underline{Z})$ 

$$\|\Psi z - \Psi w\|_{L^{p}(0,T;\underline{Z})} = \|\left(\mathbb{M}_{U}\mathcal{N}z\right)(\cdot) - \left(\mathbb{M}_{U}\mathcal{N}w\right)(\cdot)\|_{L^{p}(0,T;\underline{Z})}$$
$$\leq K_{1}\tilde{K}\|z - w\|_{L^{p}(0,T;Z)}.$$

Therefore by (4.5)  $\Psi$  is a contraction.

For the iterative scheme  $w_{n+1} = \Psi w_n$ , starting with  $w_0 = 0$ , it is seen that

$$w_1(t) = \sum_{k=1}^{m} \tilde{U}(t, \tau_k) Bu(n)_k$$

and so let  $S = \left\{ w : \|w - w_1\|_{L^p(0,T;\underline{Z})} \le \frac{K_1 \tilde{K}}{1 - K_1 \tilde{K}} \|w_1\|_{L^p(0,T;\underline{Z})} \right\}$ . S will be contained in  $B_a$  if

$$\left(1 + \frac{K_1 \tilde{K}}{1 - K_1 \tilde{K}}\right) \| \sum_{k=1}^m \tilde{U}(\cdot, \tau_k) Bu(n)_k \|_{L^p(0, T; \underline{Z})} \le a$$

which will certainly be the case if

$$\frac{1}{1 - K_1 \tilde{K}} \sqrt{m} \, K_2 \|u_n\|_U \le a$$

that is, if (4.8) is satisfied, and so applying Theorem 1 ensures the existence of a unique fixed point  $z_n$  of  $\Psi$ .

Trivially, since u(0) = 0 the inequality (4.8) is satisfied for n = 0 giving a solution  $z_0 = 0$ . Now inductively, if solutions,  $z_k(t)$ , of (4.3) exist for k < n, then

$$u(n) = (1 - \Phi^{\dagger} \Phi) u(n-1) + \Phi^{\dagger} (y_d - C\hat{z}(T) - C (\mathbb{M}_U \mathcal{N} z_{n-1}) (T))$$
  
= ... =  $\Phi^{\dagger} (y_d - C\hat{z}(T) - C (\mathbb{M}_U \mathcal{N} z_{n-1}) (T))$ 

and so

$$||u(n)||_{\mathcal{U}} \leq ||\Phi^{\dagger}|| (||y_{d} - C\hat{z}(T)||_{Y} + ||C(\mathbb{M}_{U}\mathcal{N}z_{n-1})(T)||_{Y})$$

$$\leq ||\Phi^{\dagger}|| \left(\frac{a\left(1 - K + \sqrt{m}\,\tilde{K}K_{2}||\Phi^{\dagger}||\,||C||K_{4}\right)}{\sqrt{m}\,K_{2}||B||\,||\Phi^{\dagger}||}\right) = \frac{a\left(1 - K_{1}\tilde{K}\right)}{\sqrt{m}\,K_{2}}.$$

Therefore, for each  $n \in \mathbb{N}$  there exists a solution  $z_n$  of (4.1).

Now it is shown that the iterative scheme for u(n) converges: Observe that

$$||u(m) - u(n)||_{\mathcal{U}} = ||\Phi^{\dagger}C \left( \mathbb{M}_{U}(\mathcal{N}z_{n-1} - \mathcal{N}z_{m-1}) \right) (T)||_{\mathcal{U}}$$
  
$$\leq ||\Phi^{\dagger}|| ||C|| K_{4} \tilde{K} ||z_{m-1} - z_{n-1}||_{L^{p}(0,T;Z)}$$

and so

$$||z_{m} - z_{n}||_{L^{p}(0,T;\underline{Z})} = ||\sum_{k=1}^{m} \tilde{U}(\cdot,\tau_{k})B(u(m)_{k} - u(n)_{k}) + (\mathbb{M}_{U}(\mathcal{N}z_{m} - \mathcal{N}z_{n}))(\cdot)||_{L^{p}}$$

$$\leq \frac{\sqrt{m} K_{2} ||\Phi^{\dagger}|| ||C|| K_{4} \tilde{K}}{1 - K_{1} \tilde{K}} ||z_{m-1} - z_{n-1}||_{L^{p}(0,T;\underline{Z})}.$$

Therefore, by (4.5) the sequence of solutions,  $z_n$ , (and hence controls u(n)) converges as  $n \to \infty$ . Now

$$u(n) = \Phi^{\dagger} \left( y_d - C\hat{z}(T) - C \left( \mathbb{M}_U \mathcal{N} z_{n-1} \right) (T) \right)$$

and so letting  $n \to \infty$ , since  $\Phi^{\dagger}$  and  $C(\mathbb{M}_{U})(T)$  are bounded, the limit is given by

$$u = \Phi^{\dagger} \left( y_d - C\hat{z}(T) - C \left( \mathbb{M}_U \mathcal{N} z \right) (T) \right),$$

but then z (the limit of the sequence  $(z_n)_{n\in\mathbb{N}}$ ) satisfies

$$z(t) = \sum_{k=1}^{m} \tilde{U}(t, \tau_k) B u_k + (\mathbb{M}_U \mathcal{N} z)(t), \quad u = \Phi^{\dagger} \left( y_d - C \hat{z}(T) - C \left( \mathbb{M}_U \mathcal{N} z \right)(T) \right)$$

and so is a fixed point of  $\psi$ . Hence the iterative and fixed point schemes converge to the same z and yield the same control.  $\square$ 

Consider the single input case and suppose that (as considered in [7]) the original dynamics are semilinear in form:

$$\dot{\overline{z}}(t) = f(t, \overline{z}(t)) = A\overline{z}(t) + g(t, \overline{z}(t)), \qquad \overline{z}(0) = z_0 + B\overline{u}, \tag{4.9}$$

where A is the generator of a strongly continuous semigroup, S(t), on Z and g:  $[0,T]\times Z\longrightarrow Z$  is strictly nonlinear and continuously differentiable. If an initial guess,  $\hat{u}$ , is made for the control such that  $z_0+B\hat{u}\in D(A)$ , then there exists a classical solution,  $\hat{z}(\cdot)$ , of the initial value problem on [0,T] [15]. If  $P(t)=\mathrm{d}g(\hat{z}(t))$ , the derivative of g with respect to g evaluated at  $\hat{z}(t)$ , then  $P(\cdot)\in C(0,T;\mathcal{L}(Z))$ . Define the following function from  $[0,T]\times Z\longrightarrow Z$ :

$$N(t,z) = g(t,z + \hat{z}(t)) - g(t,\hat{z}(t)) - P(t)z.$$

Therefore, setting  $\overline{z} = \hat{z} + z$  and  $\overline{u} = \hat{u} + u$  gives

$$\dot{z}(t) = (A + P(t))z(t) + N(t, z(t)), \qquad z(0) = Bu,$$

which is of the form (2.1) with  $\underline{Z} = Z = \overline{Z}$  and A(t) = A + P(t). The assumptions above ensure that  $A(\cdot) = A + P(\cdot)$  is the generator of a mild evolution operator, U(t,s), on Z that is uniformly bounded [3] (in fact U(t,s) is a weak evolution operator [9]). Therefore it is seen that assumptions TV 1–4 are satisfied.

Since g is continuously differentiable it satisfies a local Lipschitz condition in that there exists a constant  $k_*(c)$  such that

$$||g(t,z_1) - g(t,z_2)||_Z \le k_*(c)||z_1 - z_2||_Z$$

for  $z_i \in Z$  with  $||z_i||_Z \leq c$ . Therefore, the nonlinear operator  $N(\cdot, \cdot)$  is also locally Lipschitz since, for  $z_i \in Z$  with  $||z_i||_Z \leq c$ ,

$$||N(t, z_1) - N(t, z_2)||_Z \le ||g(t, z_1 + z'(t)) - g(t, z_2 + z'(t))||_Z + ||P(t)(z_1 - z_2)||_Z$$

$$\le \left(k_*(c + \eta) + \sup_{t \in [0, T]} ||P(t)||_{\mathcal{L}(Z)}\right) ||z_1 - z_2||_Z$$

where  $\eta = ||z'(\cdot)||_{C(0,T;Z)}$ .

A further control u is then sought such that, if  $\overline{z}(\cdot)$  is a solution of (4.9) with initial state

$$\overline{z}(0) = z_0 + B\hat{u} + Bu$$
.

then

$$C\overline{z}(T) = y_d$$

for some fixed T and  $y_d$ . Now consider a sequence of controls  $(u_n)_{n\in\mathbb{N}}$  that are related via the iterative scheme so that the  $n^{\text{th}}$  control,  $u_n$  is given by

$$u_n = u_{n-1} + \Phi^{\dagger}(y_d - y_{n-1}),$$

and suppose that the differential equation (4.9) can be solved for the corresponding sequence of initial states

$$\overline{z}_n(0) = z_0 + B\hat{u} + Bu_{n-1} + B\Phi^{\dagger} (y_d - y_{n-1})$$

with  $u_0 = 0$ . If the remaining conditions of Theorem 2 are satisfied then the sequence of outputs  $y_n = C\overline{z}(T)$  converges, at least on the range of  $\Phi$ , to the desired target  $y_d$ .

**5. A class of perturbed systems.** Motivated by the final remarks of the previous section consider systems in which the linear operator  $A(\cdot)$  is obtained by an unbounded perturbation of some time invariant A:

$$\dot{z}_i(t) = (A + P(t)) z_i(t) + N(t, z_i(t)), \quad z_i(\tau_i) = z_{i-1}(\tau_i) + Bu_i, \tag{5.1}$$

where  $z_0(0) = 0$ . For simplicity the degree of unboundedness of the perturbation is the same as that of the nonlinearity, and so  $P(\cdot) \in PC(0,T;\mathcal{L}(\underline{Z},\overline{Z}))$ . Based on the Pritchard-Salamon class of systems introduced in [16] to study linear quadratic optimal control for infinite-dimensional systems with unbounded input and output operators, suppose that the following assumptions hold for (5.1):

- PS 1.  $\underline{Z} \subset Z \subset \overline{Z}$  are Banach spaces such that the canonical injections  $\underline{Z} \hookrightarrow Z$ ,  $Z \hookrightarrow \overline{Z}$  are continuous with dense ranges. Moreover, the nonlinearity  $N:[0,T] \times \underline{Z} \longrightarrow \overline{Z}$  maps functions in  $L^p(0,T;\underline{Z})$  to functions in  $L^q(0,T;\overline{Z})$  for real numbers  $p \geq q \geq 1$  in the sense that  $\mathcal{N}z \in L^q(0,T;\overline{Z})$  whenever  $z \in L^p(0,T;\underline{Z})$ . In addition,  $P(\cdot) \in PC(0,T;\mathcal{L}(\underline{Z},\overline{Z}))$ .
- PS 2. A is the generator of a strongly continuous semigroup, S(t), on Z, which is also a strongly continuous semigroup on  $\underline{Z}$  and  $\overline{Z}$ .
- PS 3. There exists a continuous  $k_a(\cdot): [0,T] \longrightarrow \mathbb{R}^+$ , and for all  $s \in [0,T)$ ,  $h(\cdot) \in L^2(s,T;\overline{Z})$ , the map  $t \mapsto \int_s^t S(t-\sigma)h(\sigma)d\sigma$  is continuous from [s,T] to  $\underline{Z}$  and

$$\left\| \int_{s}^{t} S(t - \sigma) h(\sigma) d\sigma \right\|_{\underline{Z}} \le k_{a}(t - s) \|h(\cdot)\|_{L^{2}(s, t; \overline{Z})}.$$
 (5.2)

PS 4. There exists a  $K_b > 0$  such that

$$||S(\cdot)z||_{L^2(0,T;\underline{Z})} \le K_b ||z||_{\overline{Z}}$$
 (5.3)

for every  $z \in \underline{Z}$ .

In addition, the following assumption is sufficient to provide the necessary smoothing properties with respect to the possible unboundedness of the output operator C:

PS 5. There exists a Banach space  $V \subset Z$ , with continuous injection, such that  $C \in \mathcal{L}(V,Y)$ . In addition, there exist a continuous  $k_c : [0,T] \longrightarrow \mathbb{R}^+$  and a constant  $K_d$  such that for all  $s \in [0,T)$  and  $h(\cdot) \in L^2(s,T;\overline{Z})$ ,  $\int_s^T S(T-\sigma)h(\sigma)d\sigma \in V$ ,

$$\left\| \int_{s}^{T} S(T - \sigma)h(\sigma) d\sigma \right\|_{V} \le k_{c}(s) \|h(\cdot)\|_{L^{2}(s, T; \overline{Z})}$$
(5.4)

and for all k = 1, ..., m and  $u \in U$ ,  $S(T - \tau_k)Bu \in V$ ,

$$||S(T-\tau_k)Bu||_V < K_d||u||_U$$
.

Theorem 4. Suppose that conditions PS 1-3 are satisfied. Then  $A(\cdot) = A + P(\cdot)$  is the generator of a mild evolution operator U(t,s) on  $\underline{Z}$  in the sense that U(t,s) is the unique, in the class of strongly continuous operators on  $\underline{Z}$ , solution of

$$U(t,s)z = S(t-s)z + \int_{s}^{t} S(t-\sigma)P(\sigma)U(\sigma,s)zd\sigma$$
 (5.5)

for  $z \in \underline{Z}$ .

*Proof.* Fix  $s \in [0,T]$  and define an operator  $\Gamma_s: P_{\infty}(s,T;\mathcal{L}(\underline{Z})) \longrightarrow P_{\infty}(s,T;\mathcal{L}(\underline{Z}))$  by

$$\Gamma_s(U)(t)z := S(t-s)z + \int_s^t S(t-\sigma)P(\sigma)U(\sigma)z\,\mathrm{d}\sigma. \tag{5.6}$$

Note that

$$\|\Gamma_s(U_1)(t) - \Gamma_s(U_2)(t)\|_{\mathcal{L}(Z)} \le \gamma (t-s)^{1/2} \|P\| \|U_1(\cdot) - U_2(\cdot)\|_{P_{\infty}}$$

where  $K_a = \sup_{s < t < T} k_a(t-s)$  and so by induction

$$\|\Gamma_s^k(U_1) - \Gamma_s^k(U_2)\|_{P_{\infty}} \le \left\lceil \frac{(T-s)^k}{k!} \right\rceil^{1/2} (K_a \|P\|)^k \|U_1(\cdot) - U_2(\cdot)\|_{P_{\infty}}.$$

By choosing k such that  $\left[\frac{(T-s)^k}{k!}\right]^{1/2} (K_a \|P\|)^k < 1$  it is seen that  $\Gamma_s$  is a contraction on  $P_{\infty}(s,T;\mathcal{L}(\underline{Z}))$ . Therefore there exists a unique fixed point  $U(\cdot,s)$  of (5.6). This fixed point is given by  $U(t,s) = \sum_{n=0}^{\infty} U_n(t,s)$  where  $U_0(t,s)z = S(t-s)z$  and

$$U_n(t,s)z = \int_s^t S(t-\sigma)P(\sigma)U_{n-1}(\sigma,s)z\,\mathrm{d}\sigma.$$

Clearly U(s,s) = I and note that, for  $z \in \underline{Z}$ ,

$$\begin{aligned} \|U(t,r)U(r,s)z - U(t,s)z\|_{\underline{Z}} \\ &= \left\| \int_{r}^{t} S(t-\sigma)P(\sigma) \left( U(\sigma,r)U(r,s)z - U(\sigma,s)z \right) d\sigma \right\|_{\underline{Z}} \\ &\leq k_{a}(t-s)\|P\| \|(U(\cdot,r)U(r,s)z - U(\cdot,s)z)\|_{L^{2}(r,t;Z)} \,. \end{aligned}$$

Therefore, setting  $g(\alpha) = \|U(\alpha + r, r)U(r, s)z - U(\alpha + r, s)z\|_Z^2$  it follows that

$$0 \le g(t-r) \le \int_0^{t-r} [\text{const}] g(\sigma) d\sigma$$

and so applying Gromwell's Lemma U(t,s)=U(t,r)U(r,s). Suppose that  $\sup_{0\leq t\leq T}\|S(t)\|_{\mathcal{L}(\underline{Z})}=M_0,\ z\in\underline{Z}$  and consider

$$||U_{n}(t,s)z||_{\underline{Z}} \leq K_{a}||P|| ||U_{n-1}(\cdot,s)z||_{L^{2}(s,t;\underline{Z})}$$

$$\leq \left[\frac{(t-s)^{n}}{n!}\right]^{1/2} (K_{a}||P||)^{n} M_{0}||z||_{\underline{Z}}.$$

Therefore the series giving U(t,s) is majorised by

$$M_0 \sum_{n=0}^{\infty} \left[ \frac{(t-s)^n}{n!} \right]^{1/2} (K_a ||P||)^n$$

and so converges absolutely in the uniform topology of  $\mathcal{L}(\underline{Z})$ . Thus  $U(\cdot, \cdot)$  is uniformly bounded, with bound denoted by  $\underline{M}_U$ . Together with the strong continuity of S(t) this implies that  $U(\cdot, \cdot)$  is strongly continuous on  $\Delta(T)$ .  $\square$ 

In fact the smoothing properties of the semigroup, PS 3 and PS 4, are sufficient for U(t,s) to be extended to a mild evolution operator on Z and  $\overline{Z}$ :

COROLLARY 1. Suppose that the hypotheses of Theorem 4, together with PS 4, are satisfied and let U(t,s) be the corresponding mild evolution operator. Then an extension of U(t,s) to a bounded linear operator on  $\overline{Z}$  can be defined by

$$\tilde{U}(t,s)z := \lim_{n \to \infty} U(t,s)z_n$$

for each  $z \in \overline{Z}$ , where  $(z_n)_{n=1}^{\infty}$  is a sequence into  $\underline{Z}$  such that  $||z_n - z||_{\overline{Z}} \to 0$  as  $n \to \infty$ . Furthermore, this extension, which will be denoted by U(t,s), is a mild evolution operator on Z and  $\overline{Z}$ .

*Proof.* First note that there exist positive constants,  $R_1$  and  $R_2$ , such that  $||z||_{\overline{Z}} \le R_1||z||_Z \le R_1R_2||z||_{\overline{Z}}$  for all  $z \in \underline{Z}$ . Let  $z \in \underline{Z}$  and consider

$$||U_{n+1}(t,s)z||_{\underline{Z}} \le K_a ||P|| ||U_n(\cdot,s)z||_{L^2(s,t;\underline{Z})}$$

$$\le \left[\frac{(t-s)^n}{n!}\right]^{1/2} (K_a ||P||)^{n+1} K_b ||z||_{\overline{Z}}$$

so that there exists a constant,  $M_1$ , such that  $||U(t,s)z||_{\underline{Z}} \leq M_1||z||_{\overline{Z}}$  for all  $z \in \underline{Z}$ . Therefore it is seen that  $U(\cdot,\cdot)$  is uniformly bounded with respect to  $||\cdot||_Z$  and  $||\cdot||_{\overline{Z}}$ , with bounds denoted by  $M_U$  and  $\overline{M}_U$ .

Now for  $z \in \overline{Z}$ , let  $(z_n)_{n=1}^{\infty}$  be a sequence into  $\underline{Z}$  such that  $||z_n - z||_{\overline{Z}} \to 0$ . Then

$$\|\tilde{U}(t,s)z\|_{\overline{Z}} = \lim_{n \to \infty} \|U(t,s)z_n\|_{\overline{Z}} \le \lim_{n \to \infty} \overline{M}_U \|z_n\|_{\overline{Z}} = \overline{M}_U \|z\|_{\overline{Z}}$$

and so the extension of U(t,s) to  $\overline{Z}$  (and Z) is also uniformly bounded. It is clear that  $\tilde{U}(t,t)z=z$  for all  $z\in\overline{Z}$ , and if  $(t,s)\in\Delta(T)$ , with  $r\in[s,t]$ , then

$$||U(t,r)U(r,s)z_n - \tilde{U}(t,s)z||_{\overline{Z}} = ||\tilde{U}(t,s)z_n - \tilde{U}(t,s)z||_{\overline{Z}} \le \overline{M}_U ||z_n - z||_{\overline{Z}} \longrightarrow 0$$

as  $n \to \infty$ . Therefore  $\tilde{U}(t,s)z = \tilde{U}(t,r)\tilde{U}(r,s)z$  for all  $z \in \overline{Z}$ .

To see that  $U(\cdot,\cdot)$  is strongly continuous note that

$$\|\tilde{U}(t,s)z - U(t,s)z_n\|_{\overline{Z}} = \|\tilde{U}(t,s)z - \tilde{U}(t,s)z_n\|_{\overline{Z}} \leq \overline{M}_U\|z_n - z\|_{\overline{Z}}$$

and so  $\tilde{U}(\cdot,s)z$  is the uniform limit of a sequence of continuous functions,  $U(\cdot,s)z_n$ . Similarly,  $\tilde{U}(t,\cdot)z$  is also continuous and the extension  $\tilde{U}(t,s)$  is a mild evolution operator on Z and  $\overline{Z}$ , which will be denoted by U(t,s) in the following.  $\square$ 

REMARK 2. In proving the uniform boundedness of the mild evolution operator in Corollary 1 it is seen that there exists a constant  $M_1$  such that  $||U(t,s)z||_{\underline{Z}} \leq M_1||z||_{\overline{Z}}$  for all  $z \in \underline{Z}$ . Therefore the extension to  $\overline{Z}$  satisfies  $U(t,s) \in \mathcal{L}(\overline{Z},\underline{Z})$  with uniform bound  $M_1$ . Hence U(t,s) satisfies TV 3. Moreover,  $||U(t,s)Bu||_{\underline{Z}} \leq R_1 M_1 ||B|| ||u||_U$  for all  $u \in U$  so that TV 4 is also satisfied.

Remark 3. Note that if PS 5 is satisfied then for all  $z \in \underline{Z}$ 

$$\left\| \int_{s}^{T} S(T-\sigma)P(\sigma)U(\sigma,s)z \,d\sigma \right\|_{V} \le k_{c}(s)(T-s)^{1/2}\|P\|M_{1}\|z\|_{\overline{Z}}.$$

Thus it is seen that the extension of  $z \mapsto \int_s^T S(T - \sigma)P(\sigma)U(\sigma, s)z \,d\sigma$  to a bounded map from  $\overline{Z}$  to  $\underline{Z}$  also maps into V. Furthermore, this extension is strongly continuous in s with respect to  $\mathcal{L}(\overline{Z}, V)$ .

Suppose that A is the generator of a semigroup S(t) such that assumptions PS 1–PS 5 are satisfied. Assumption TV 1 is the same as PS 1, while the previous results show that  $A + P(\cdot)$  is the generator of a mild evolution operator U(t,s) on  $\underline{Z}$ , Z and  $\overline{Z}$  so that TV 2–4 are satisfied. Now let  $h \in L^q(0,T;\overline{Z})$  and consider

$$\mapsto \int_{s}^{T} S(T - \sigma) P(\sigma) U(\sigma, s) h(s) d\sigma,$$

which is measurable from Remark 3. Furthermore, this map is integrable in V:

$$\int_{0}^{T} \left\| \int_{s}^{T} S(T - \sigma) P(\sigma) U(\sigma, s) h(s) d\sigma \right\|_{V} ds$$

$$\leq \int_{0}^{T} K_{c}(T - s)^{1/2} \|P\| M_{1} \|h(s)\|_{\overline{Z}} ds \leq K_{c} \|P\| M_{1} T^{1/2} T^{1/\hat{q}} \|h(\cdot)\|_{L^{q}(0, T; \overline{Z})}$$

where  $K_c = \sup_{0 \le t \le T} k_c(t)$  and  $(1/\hat{q}) + (1/q) = 1$ . Since  $\int_s^T S(T - \sigma)h(\sigma)d\sigma \in V$  by assumption it follows that  $(\mathbb{M}_U h)(T) \in V$ . Note that

$$\left\| \int_0^T U(T,s)h(s) \, \mathrm{d}s \right\|_V$$

$$\leq \left\| \int_0^T S(T-s)h(s) \, \mathrm{d}s \right\|_V + \left\| \int_0^T \int_s^T S(T-\sigma)P(\sigma)U(\sigma,s)h(s) \, \mathrm{d}\sigma \mathrm{d}s \right\|_V$$

$$\leq K_c \left( 1 + \|P\|M_1 T^{1/2} T^{1/\hat{q}} \right) \|h(\cdot)\|_{L^q(0,T;\overline{Z})}.$$

In addition, for  $u \in U$  and  $1 \le k \le m$ 

$$||U(T,\tau_k)Bu||_V \le \left(K_d + K_c T^{1/2} ||P|| M_1 R_1 ||B||\right) ||u||_U$$

and so TV 5 is also satisfied.

The preceding discussion shows that for a perturbed system such that assumptions PS 1–PS 5 hold, a mild evolution operator is defined for which TV 1–TV 5 are satisfied. Hence the methods of the previous sections can be applied.

Example. Consider the following diffusion equation with simple nonlinearity:

$$\frac{\partial \overline{z}}{\partial t} = \frac{\partial^2 \overline{z}}{\partial x^2} + \overline{z}^2, \qquad \overline{z}(0,t) = \overline{z}(1,t) = 0$$

such that the input acts via the initial condition,  $\overline{z}(x,t) = \overline{u}(x)$ . This example is considered with respect to the Hilbert space  $Z = L^2(0,1)$  as the abstract differential equation

$$\dot{\overline{z}} = A\overline{z} + \overline{z}^2, \qquad \overline{z}(0) = \overline{u}$$

where  $Ah = \frac{\mathrm{d}^2 h}{\mathrm{d}x^2}$  for  $h \in D(A) = \{h \in L^2(0,1) : h, \frac{\mathrm{d}h}{\mathrm{d}x} \text{ are absolutely continuous, } \frac{\mathrm{d}^2 h}{\mathrm{d}x^2} \in L^2(0,1) \text{ and } h(0) = h(1) = 0\}$ . Then A is the generator of a strongly continuous semi-group S(t) on Z given by

$$S(t)z = \sum_{n=1}^{\infty} e^{-n^2 \pi^2 t} \langle \psi_n, z \rangle_Z \psi_n$$

where  $\psi_n(x) = \sqrt{2}\sin(n\pi x)$  is an orthonormal basis for  $Z = L^2(0,1)$ . With respect to this basis and any real  $\alpha > 0$  define the following dense linear subspace of Z:

$$Z_{\alpha} := \left\{ z \in Z : \sum_{n=1}^{\infty} n^{2\alpha} \langle \psi_n, z \rangle_Z^2 < \infty \right\}$$

with corresponding inner product

$$\langle z_1, z_2 \rangle_{\alpha} := \sum_{n=1}^{\infty} n^{2\alpha} \langle \psi_n, z_1 \rangle_Z \langle \psi_n, z_2 \rangle_Z.$$

The space  $Z_{\alpha}$  is a Hilbert space under this inner product.

Since the nonlinearity is continuously differentiable on  $L^{\infty}(0,1)$  then  $\hat{u} \in D(A)$  gives rise to a classical solution,  $\hat{z}$ , on  $L^{\infty}(0,1)$ . Now consider the perturbations  $\overline{z} = z + \hat{z}$  and  $\overline{z} = u + \hat{u}$ :

$$\dot{z}(t) = Az(t) + 2\hat{z}(t)z(t) + z(t)^2, \qquad z(0) = u.$$

Therefore this system is of the form considered in this section where  $P(t)z := 2\hat{z}(t)z$  and  $N(z) = z^2$ . The problem is to determine  $u \in U = Z_\beta$  ( $\beta \ge 2$  so that  $U \subseteq D(A)$ ) such that  $z(T) + \hat{z}(T)$  is some desired target  $y_d$ . Therefore the output is y = z(T) so that C = 1 and  $Y = Z = L^2(0, 1)$ .

Choose  $\underline{Z} = Z_{\alpha}$ , with  $\alpha > \frac{1}{2}$  so that  $Z_{\alpha} \subset L^{\infty}(0,1)$ , and  $\overline{Z} = Z$ . Then  $P(\cdot) \in C(0,T;\mathcal{L}(\underline{Z},Z))$ , and  $N:\underline{Z} \longrightarrow Z$  is such that  $N(z(\cdot)) \in L^2(0,T;Z)$  whenever  $z(\cdot) \in L^4(0,T;\underline{Z})$ . The nonlinearity satisfies the Lipschitz condition (3.7) with  $k(\theta_1,\theta_2) = m_3(\theta_1 + \theta_2)$  for a constant  $m_3$ . Then it is seen that the semigroup generated by S(t) satisfies assumptions PS 1 and PS 2.

For  $z(\cdot) \in L^2(0,T;Z)$  and  $(\frac{1}{2} <) \alpha \le 1$  consider

$$\left\| \int_{s}^{t} S(t - \sigma) z(\sigma) d\sigma \right\|_{\alpha}^{2} = \sum_{n=1}^{\infty} n^{2\alpha} \left[ \int_{s}^{t} e^{-n^{2}\pi^{2}(t - \sigma)} \langle \psi_{n}, z(\sigma) \rangle_{Z} d\sigma \right]^{2}$$

$$\leq \frac{1}{2\pi^{2}} \left( 1 - e^{-2\pi^{2}(t - s)} \right) \sum_{n=1}^{\infty} n^{2(\alpha - 1)} \left[ \int_{s}^{t} \langle \psi_{n}, z(\sigma) \rangle_{Z}^{2} d\sigma \right]$$

$$\leq \frac{1}{2\pi^{2}} \left( 1 - e^{-2\pi^{2}(t - s)} \right) \int_{s}^{t} \|z(\sigma)\|_{Z}^{2} d\sigma$$

so that (5.2) is satisfied with  $k_a(t) = \frac{1}{\sqrt{2}\pi} \left(1 - e^{-2\pi^2 t}\right)^{1/2}$  and PS 3 is satisfied. Now for  $z \in \mathbb{Z}$  note that

$$\sum_{n=1}^{\infty} \left( \int_{0}^{T} n^{2\alpha} e^{-2n^{2}\pi^{2}t} \langle \psi_{n}, z \rangle_{L^{2}}^{2} \right) dt \le \frac{1}{2\pi^{2}} \left( 1 - e^{-2\pi^{2}T} \right) \|z\|_{Z}^{2} < \infty$$

so that

$$\int_0^T \left( \sum_{n=1}^\infty n^{2\alpha} \mathrm{e}^{-2n^2\pi^2t} \langle \psi_n, z \rangle_{L^2}^2 \mathrm{d}t \right) \\ = \sum_{n=1}^\infty \left( \int_0^T n^{2\alpha} \mathrm{e}^{-2n^2\pi^2t} \langle \psi_n, z \rangle_{L^2}^2 \right) \mathrm{d}t$$

and hence the series converges for almost all  $t \in [0, T]$ . Hence

$$||S(\cdot)z||_{L^2(0,T;Z_\alpha)}^2 \le \frac{1}{2\pi^2} \left(1 - e^{-2\pi^2 T}\right) ||z||_Z^2$$

and PS 4 is satisfied with  $K_b = \frac{1}{2\pi^2} \left( 1 - e^{-2\pi^2 T} \right)^{1/2}$ .

Considering the special case where  $\hat{u}=0$  so that  $\hat{z}(t)=0$  it is seen that the linear operator  $\phi:U\longrightarrow Y$  is such that

$$\phi u = \sum_{n=1}^{\infty} e^{-n^2 \pi^2 T} \langle \psi_n, u \rangle_{L^2} \psi_n$$

and therefore

$$\operatorname{ran} \phi = R(\phi) := \left\{ y \in Z : \sum_{n=1}^{\infty} n^{2\beta} e^{2n^2 \pi^2 T} \langle \psi_n, y \rangle_Z^2 < \infty \right\}.$$

Since ran  $\phi$  is a dense linear subspace of Y it is seen that the linearised system is approximately controllable to Y=Z, but ran  $\phi$  is not a closed subspace of Y. The most natural restriction of Y is to the Hilbert space  $R(\phi)$ , in which case  $V=R(\phi)$ . However, in this case it is not possible to verify assumption PS 5, and so constraining attention to the space controllable to from the initial condition for the linearised system is too restricting.

An alternative approach is to restrict U to a finite dimensional subspace of U: For any  $m \in \mathbb{N}$  let  $U_m = \{u \in U : u = \sum_{n=1}^m u_n n^{-\beta} \psi_n, u_n \in \mathbb{R}\}$ , which is isomorphic to  $\mathbb{R}^m$ . With respect to this input space the linear operator  $\phi_m : U_m \longrightarrow Y$  is such that

$$\phi_m u = \sum_{n=1}^m u_n e^{-n^2 \pi^2 T} n^{-\beta} \psi_n,$$

and so ran  $\phi_m$  is a closed subspace of Y that is also isomorphic to  $\mathbb{R}^m$ . Note that the generalised inverse of  $\phi_m$  can be explicitly constructed as a map from Y to  $U_m$ :

$$\Phi_m^{\dagger} y = \sum_{n=1}^m \left[ e^{n^2 \pi^2 T} n^{\beta} \langle \psi_n, y \rangle_Z \right] n^{-\beta} \psi_n = \sum_{n=1}^m e^{n^2 \pi^2 T} \langle \psi_n, y \rangle_Z \psi_n.$$

If V=Z then PS 5 is satisfied since  $Z=\overline{Z}$  and S(t) is a strongly continuous semigroup on Z. Since  $e^{-n^2\pi^2T}n^{-\beta}\psi_n$  forms an orthonormal basis of  $R(\phi)$  with respect to the inner product

$$\langle y_1, y_2 \rangle_{R(\phi)} = \sum_{n=1}^{\infty} e^{2n^2 \pi^2 T} n^{2\beta} \langle \psi_n, y_1 \rangle_Z \langle \psi_n, y_2 \rangle_Z,$$

any  $y_d \in \operatorname{ran} \phi$  can be approximated by  $y_{d,m}$  given by

$$y_{d,m} = \sum_{n=1}^{m} e^{-n^2 \pi^2 T} n^{-\beta} \langle \psi_n, y_d \rangle_Z \psi_n \in \operatorname{ran} \phi_m.$$

The results of Sections 3 and 4 can therefore be applied to determine a control  $u_m$  that drives the system to  $y_{d,m}$  on ran  $\phi_m$ .

6. Application: Control of viral load in HIV. The quantitative predictions of the consequences of various dosing regimens for a pharmaceutical intervention can be provided by a validated pharmacokinetic (PK) model, which describes the absorption, distribution, metabolism and excretion of the agent. Properties of the time course (such as half-life or area-under-curve, AUC) for a particular compartment (typically blood plasma) might be linked to pharmacological activity, or directly modelled by coupling the PK model with a pharmacodynamic (PD) model of the physiological effect of the agent.

The high replication and mutation rates of the human immunodeficiency virus (HIV), which ultimately results in strains resistant to any single agent, leads to the adoption of a multiple-agent strategy. Highly active anti-retroviral therapy (HAART) uses two or more agents that target different components of the HIV replication cycle, but these agents typically produce adverse side effects in patients. A number of authors have applied techniques from nonlinear control to this problem, but in general the explicit link between the drug dose and the physiological effect, via the PK, is neglected so that the controls derived are continuous in time. In the finite-deminsional case, Mhawej et al. [13] addressed this control problem via feedback linearization applied to a PD model of HIV dynamics. A single-compartment PK model was then used to estimate a dosing regime that gave rise to the required continuous control law. The general dosing problem for finite-dimensional systems was considered in [6] in which a fixed-point approach was taken to determine the doses required to obtain a particular AUC or target profile.

Dixit and Perelson [5] argue that the viral dynamics for HIV should include an intracellular delay between infection of cells and production of new virus. In the presence of a reverse transcriptase inhibitor (RTI) the corresponding delayed differential system for the viral dynamics is given by the following [5]:

$$\dot{x}_1(t) = p_1 - p_2 x_1(t) - (1 - \epsilon(t)) p_3 x_1(t) x_3(t) 
\dot{x}_2(t) = (1 - \epsilon(t - \tau)) p_4 x_1(t - \tau) x_3(t - \tau) - p_5 x_2(t) 
\dot{x}_3(t) = p_6 x_2(t) - p_7 x_3(t)$$
(6.1)

where  $p_i > 0$  are parameters,  $\tau$  is a fixed intracellular delay,  $x_1(t)$  is the density of uninfected CD4+ T cells,  $x_2(t)$  the corresponding density of infected T cells and  $x_3(t)$  is the viral load. The efficacy of the RTI is represented by  $\epsilon$  and related to drug plasma concentration,  $C_p(t)$ , by the following:

$$\epsilon(t) = \frac{C_p(t)}{IC_{50} + C_p(t)} = \frac{x_4(t)}{v_P IC_{50} + x_4(t)}$$

where  $IC_{50}$  is the plasma concentration required to achieve 50% efficacy,  $v_P$  is the plasma volume of distribution and  $x_4(t)$  the mass of drug in plasma. For simplicity the efficacy is related directly to plasma concentration rather than intracellular concentration (the latter as was done in [5]). Assuming standard oral absorption kinetics for the RTI the drug plasma concentration is related to the dose, D, via the following two-compartment model:

$$\dot{G}(t) = -k_A G(t), \qquad G(0) = g_0 + fD 
\dot{x}_4(t) = k_A G(t) - k_{EL} x_4(t), \qquad x_4(0) = m_0$$
(6.2)

where G(t) is the mass of drug in the gut, f is the drug bioavailability,  $k_A$  the absorption rate constant and  $k_{EL}$  the elimination rate constant.

The general control problem associated with models of this form is to choose daily dosages in order to reduce viral load a certain amount in the short-term and then below a detectability limit in the medium to long-term (see, for example, [13]). Therefore, consider the problem of determining doses  $D_i$  (i = 1, ..., m), administered at times  $\tau_i$ , such that the viral load is some prescribed trajectory. For convenience the PK model (6.2) is replaced by the following polynomial version:

$$\dot{x}_4(t) = k_A \sum_{i=1}^m x_{5+i}(t - \tau_i) - k_{EL}x_4(t), \quad x_4(0) = 0$$

$$\dot{x}_5(t) = -x_5(t)^2 \left( k_A \sum_{i=1}^m x_{5+i}(t - \tau_i) - k_{EL}x_4(t) \right), \quad x_5(0) = 1/(v_P I C_{50})$$

$$\dot{x}_{5+i}(t) = -k_A x_{5+i}(t), \quad x_{5+i}(0) = f D_i, \quad i = 1, \dots, m,$$
(6.3)

so that  $\epsilon(t) = x_4(t)x_5(t)$ .

It is assumed that the first dose corresponds to  $\tau_1 = 0$ , so that for t < 0 no drug is present in the system, and it is also assumed that the virus dynamics are in steady state prior to administration. This system is therefore of the form

$$\dot{x}(t) = A_0 x(t) + \sum_{i=2}^{m} A_i x(t - \tau_i) + g(x(t), x(t - \tau), x(t - \tau_2), \dots, x(t - \tau_m)), x(0) = x_0 + B\overline{u}$$

where 
$$\overline{u} = (D_1, \dots, D_m)^T \in U = \mathbb{R}^m$$
 and  $g : \mathbb{R}^n \times \dots \times \mathbb{R}^n \longrightarrow \mathbb{R}^n$  is given by

$$g(x, x^{\tau}, x^{\tau_2}, \dots, x^{\tau_m}) = \left(p_1 - p_3(1 - x_4 x_5) x_1 x_3, p_4(1 - x_4^{\tau} x_5^{\tau}) x_1^{\tau} x_3^{\tau}, 0, 0, -x_5^2 \left(k_A x_6 + k_A \sum_{i=2}^m x_{5+i}^{\tau_i} - k_{EL} x_4\right), 0, \dots, 0\right)^T.$$

The state for the abstract differential equation formulation is  $\overline{z}(t) = (\overline{z}_1(t), \overline{z}_2(t))^T$ , where  $\overline{z}_1(t) = x(t)$  and  $[\overline{z}_2(t)](\theta) = x(t+\theta)$  for  $\theta \in [-\tau_m, 0]$ . The Banach space Z is taken to be  $\mathbb{R}^n \times C(-\tau_m, 0; \mathbb{R}^n)$  for n = 5 + m. The corresponding system equation is given by

$$\dot{\overline{z}}(t) = \mathcal{A}\overline{z}(t) + \mathcal{G}(\overline{z}(t)) \qquad \overline{z}(0) = \overline{z}_0 + \mathcal{B}\overline{u}$$
(6.4)

where

$$\mathcal{A}\left(\frac{\overline{z}_1}{\overline{z}_2(\cdot)}\right) = \begin{pmatrix} A_0\overline{z}_1(t) + \sum_{i=2}^m A_i\overline{z}_2(-\tau_i) \\ \frac{d\overline{z}_2}{d\theta}(\cdot) \end{pmatrix}$$

with domain

$$D(\mathcal{A}) = \left\{ \begin{pmatrix} \overline{z}_1 \\ \overline{z}_2(\cdot) \end{pmatrix} \in Z : \overline{z}_2(\cdot) \in C^1(-\tau_m, 0; \mathbb{R}^n) \text{ and } \overline{z}_2(0) = \overline{z}_1 \right\}.$$

and

$$\mathcal{G}\begin{pmatrix} \overline{z}_1 \\ \overline{z}_2(\cdot) \end{pmatrix} = \begin{pmatrix} g(\overline{z}_1, \overline{z}_2(-\tau), \overline{z}_2(-\tau_2), \dots, \overline{z}_2(-\tau_m)) \\ 0 \end{pmatrix} \qquad \mathcal{B}\overline{u} = \begin{pmatrix} B\overline{u} \\ 0 \end{pmatrix}.$$

Note that A is the generator of a strongly continuous semigroup on Z that is defined by:

$$S(t) \begin{pmatrix} x(0) \\ h(\cdot) \end{pmatrix} = \begin{pmatrix} x(t) \\ x(t+\cdot) \end{pmatrix} \quad \text{where } x(\theta) = h(\theta) \text{ for } \theta \in [-\tau_m, 0].$$

Let  $T > \tau_m$  and consider the problem of choosing  $\overline{u}$  such that the output is the viral load over the final  $\tau_m$  units of time, which is given by

$$y = C\overline{z}(T)$$
 where  $C\binom{r}{h(\cdot)} = h_3(\cdot) \in Y = L^2(-\tau_m, 0; \mathbb{R}),$  (6.5)

is some given function  $y_d$ . Note that  $C \in \mathcal{L}(Z, Y)$ .

If an initial guess,  $\hat{u}$ , is made for the vector of doses, which gives rise to a classical solution,  $\hat{z}(t)$ , then

$$\dot{z}(t) = (\mathcal{A} + \mathcal{P}(t)) z(t) + N(t, z(t)), \qquad z(0) = \mathcal{B}u$$

where  $\mathcal{P}(t)z = d\mathcal{G}(\hat{z}(t))z$  ( $d\mathcal{G}(\hat{z}(t))$  is the derivative of  $\mathcal{G}(\cdot)$  evaluated at  $\hat{z}(t)$ ) and, for  $z = (r, h(\cdot))^T$ ,

$$N(t,z) = \mathcal{G}(z+\hat{z}(t)) - \mathcal{G}(\hat{z}(t)) - \mathcal{P}(t)z$$

$$= \left(-p_3 M_1(r,\hat{x}(t)), p_4 M_1(h(-\tau),\hat{x}(t-\tau)), 0, 0, -M_2(z,\hat{z}(t)), 0, \dots, 0\right)^T$$

with

$$M_1(w,v) = (1 - v_4v_5) w_1w_3 - (v_5w_4 + v_4w_5 + w_4w_5) (v_1w_3 + v_3w_1 + w_1w_3) - v_1v_3w_4w_5$$

$$M_2(z, \hat{z}(t)) = (r_5^2 + 2\hat{x}_5(t)r_5) \left( k_A r_6 + k_A \sum_{i=2}^m h_{5+i}(-\tau_i) - k_{EL} r_4 \right) + r_5^2 \left( k_A \hat{x}_6(t) + k_A \sum_{i=2}^m \hat{x}_{5+i}(t - \tau_i) - k_{EL} \hat{x}_4(t) \right).$$

Since  $\mathcal{P}(\cdot) \in C(0,T;\mathcal{L}(Z))$ ,  $\mathcal{A} + \mathcal{P}(\cdot)$  is the generator of a uniformly bounded weak evolution operator, U(t,s), on Z. With  $p=q=\infty$  and V=Z assumptions TV 1–5 are satisfied.

Since U is finite dimensional the range of the linear operator  $\phi u = CU(T,0)\mathcal{B}u$  is a closed subspace of Y. The nonlinearity  $N(\cdot,\cdot)$  satisfies the Lipschitz condition with

$$k(\theta_1, \theta_2) = m_4 \left(\theta_1 + \theta_2 + \theta_1^2 + \theta_2^2 + \theta_1^3 + \theta_2^3\right)$$

for a suitable constant  $m_4$ . Thus the iterative approach of Section 4 is applied in MATLAB, with the system equations numerically solved using the delayed differential equation solver (dde23) using the parameter values provided in [5].

The problem is considered over a period of 30 days with daily dosing, so that  $\tau_i = i-1$  (days) and T=30 (days). In Figure 6.1 the viral load corresponding to a standard treatment of 300 mg daily is shown. It is noticeable from this figure that viral load increases after approximately 20 days. To improve on the standard treatment response the target for the control scheme is chosen to be a decaying exponential (to

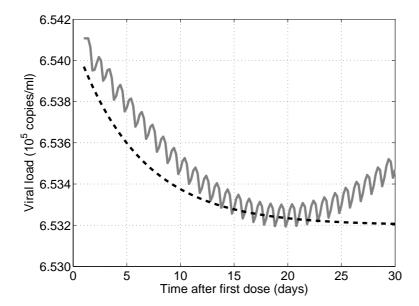


Fig. 6.1. Viral load following standard treatment protocol of 300 mg per day (solid line) and decaying exponential target for control scheme (dashed line).

a baseline) that approximates the first 20 days of standard treatment, as indicated in Figure 6.1.

Starting with an initial dose,  $\hat{u}$ , corresponding to a treatment schedule of 150 mg daily the iterative scheme produces a dosing schedule shown in Figure 6.2, which results in the viral load shown in Figure 6.3. Starting from other constant levels for the initial dose does not significantly affect the final control obtained. The iterative scheme was also applied to the target given by

$$\tilde{y}_d = \phi \phi^{\dagger} \left( y_d - C\hat{z}(T) \right) + C\hat{z}(T) = \phi \phi^{\dagger} y_d + \left( 1 - \phi \phi^{\dagger} \right) C\hat{z}(T)$$

so that  $\tilde{y}_d - C\hat{z}(T) \in \operatorname{ran} \phi$ . The dosing schedule returned is not significantly different from that in Figure 6.2 but it is seen that the response converges to the output  $y_d$ , as seen in Figure 6.4. This modified target is dependent on the initial dosing schedule,  $\hat{u}$ , both in terms of the dependence of  $\phi$  on  $\hat{z}$ , but also in terms of the presence of the term  $C\hat{z}(T)$ .

7. Conclusions. A control problem has been considered for nonlinear time-varying distributed parameter systems, in which the control acts only via part of the initial state. The problem was to drive part, or all, of the process to some desired state in a specified time. The approach taken was to formulate the problem as a fixed point one for a suitably defined abstract differential equation, with conditions imposed such that it is well defined while allowing for unboundedness of the nonlinearity in the system. Under additional conditions a version of the Contraction Mapping Theorem could be applied that yielded a solution to a weakened version of the original problem. The solution obtained ensures that the target state is achieved on the range of a linear operator arising from a linearisation of the system about an initial estimate for the control, which suggests that the initial control be chosen carefully.

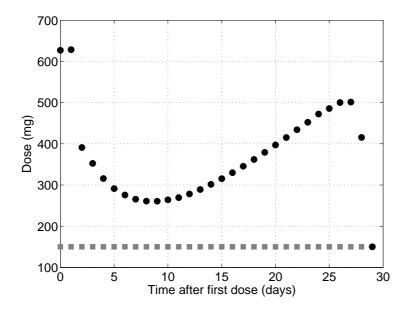


Fig. 6.2. Dosing schedule returned by iterative scheme (circles) starting from initial schedule of 150 mg per day (squares).

Application of the Contraction Mapping Theorem yields a constructive method to determine the required fixed point solution, and from this the required control is obtained. However, this approach involves integral equations that require the full solution trajectory at each step to be stored. Therefore, an alternative, more direct, approach was presented, in which an iterative scheme for the control is implemented that uses the original system dynamics. The same conditions for the fixed point approach are required and the iterative scheme yields the same solution, though in this case the required control is directly constructed. If a solution to the original problem exists, which yields the required target trajectory, it remains to be determined whether the fixed point approach presented here determines it.

The applicability of the iterative scheme for constructing the required control was illustrated by considering the problem of determining a dosing schedule for the control of HIV dynamics. The model for the viral dynamics of HIV in patients proposed by Dixit and Perelson [5] includes an intracellular delay parameter and was coupled with a two compartment model for the pharmacokinetics of a reverse transcriptase inhibitor, via saturable nonlinear pharmacodynamic term relating efficacy (within the HIV dynamics model) to plasma drug concentration. Exploiting the time-delay form of the equations a series of oral drug administrations was included in the initial state of the system model. The control produced by the iterative scheme drove the system to a particular trajectory corresponding to the orthogonal projection of the output corresponding to the initial control onto the orthogonal complement of the range.

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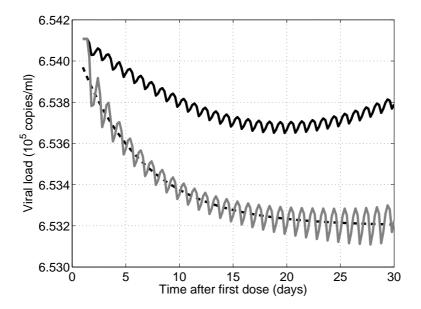


FIG. 6.3. Decaying exponential target for control scheme (dashed black line), viral load following initial dosing schedule of 150 mg per day (solid black line), and viral load following dosing schedule produced by iterative scheme (solid grey line).

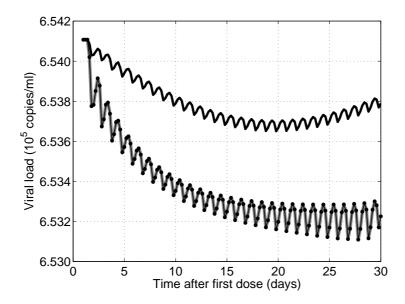


Fig. 6.4. Modified target for control scheme (solid grey line), viral load following initial dosing schedule of 150 mg per day (solid black line), and viral load following dosing schedule produced by iterative scheme (black circles).

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