Letter to the Editors

Topology selection by chaotic neurons of a pyloric central pattern generator

R. Huerta\textsuperscript{1,2}, P. Varona\textsuperscript{1,2}, M. I. Rabinovich\textsuperscript{2}, Henry D. I. Abarbanel\textsuperscript{2,3}

\textsuperscript{1} GNB. Escuela Técnica Superior de Informática, Universidad Autónoma de Madrid, 28049 Madrid, Spain
\textsuperscript{2} Institute for Nonlinear Science, University of California San Diego, La Jolla, CA 92093-0402, USA
\textsuperscript{3} Department of Physics and Marine Physical Laboratory, Scripps Institution of Oceanography, University of California San Diego, La Jolla, CA 92093-0402, USA

Received: 5 July 2000 / Accepted in revised form: 16 October 2000

Abstract. The pyloric Central Pattern Generator (CPG) in the lobster has an architecture in which every neuron receives at least one connection from another member of the CPG. We call this a “non-open” network topology. An “open” topology, where at least one neuron does not receive synapses from any other CPG member, is found neither in the pyloric nor in the gastric mill CPG. Here we investigate a possible reason for this topological structure using the ability to perform a biologically functional task as a measure of the efficacy of the network. When the CPG is composed of model neurons that exhibit regular membrane voltage oscillations, open topologies are as able to maximize this functionality as non-open topologies. When we replace these models by neurons which exhibit chaotic membrane voltage oscillations, the functional criterion selects non-open topologies. As isolated neurons from invertebrate CPGs are known in some cases to undergo chaotic oscillations, this suggests that there is a biological basis for the class of non-open network topologies that we observe.

1 Introduction

Central Pattern Generator (CPG) neural networks perform a wide variety of functional roles, each of them requiring rhythmic output from the CPG to the muscles that control the function (Marder and Calabrese, 1996; Selverston 1999). In our study of the pyloric CPG of the California spiny lobster \textit{Panulirus interruptus}, we have addressed the question of why the network is non-open in the sense that all neurons in the CPG receive input from other neurons in the circuit. The pyloric CPG is illustrated in the right half of Fig. 1A. Although in the present work we studied a system inspired by the pyloric system of the lobster, it is remarkable to note that non-open topologies are found in many CPGs, as shown in Fig. 1.

The pyloric CPG is composed of a set of neurons that are connected through specific synapses. These neurons produce a spiking-bursting activity that keeps a characteristic phase relationship between the bursts of other members due, mainly, to the synaptic connection topology of the CPG (Selverston and Moulins 1987). The electrical activity of the neurons in the CPG is propagated to the muscles, where the spikes are integrated to exert force on different places of a mechanical device or plant. The device to be controlled by the CPG is the pyloric chamber of the lobster by means of the muscles. The pyloric CPG has as its main task the transport of shredded food from the stomach to the digestive system.

In order to understand the existence of the non-open topologies, we use two different types of model neurons: conductance-based Hodgkin-Huxley (HH) (Hodgkin and Huxley 1952) neurons with periodic behavior, and chaotic Hindmarsh-Rose (HR) (Hindmarsh and Rose 1984) neurons. We study whether the CPG works well and is stable by evaluating the functionality that it accomplishes. The functional criterion for the selection of network topologies is the ability to perform the transport of fluid through the pyloric chamber. We summarize our goal as the analysis of the capability to provide efficient flow of fluid by the CPG rhythm as a function of regular versus chaotic neurons and open versus non-open connection topologies.

An important issue in all our simulations is that noise and different initial conditions are utilized to test robustness. Therefore, both efficiency of the transport and robustness are the measures subjected to study. The simulations that we present in this work show that:

1. If chaotic neurons are placed in the nodes of the CPG, only non-open topologies produce a stable and efficient accomplishment of the task.
2. If periodic neurons are employed, both open and non-open topologies achieve a stable and efficient goal.

One of the motivations of the work presented here is the observation that individual neurons of the pyloric CPG

Correspondence to: R. Huerta (e-mail: ramon.huerta@ii.uam.es)
are irregular, non-periodic, or chaotic in their membrane voltage activity (Elsom et al., 1999; Abarbanel et al. 1996). This leads to the question of how such neurons can be combined in an efficient and robust fashion to perform the job of providing rhythmic voltage output to muscles. This is, of course, the job of all CPGs, and so our question is cast broadly.

In this paper we explore one aspect of this question, that of recognizing that the network properties are determined by the component neurons, by the topology of the connections, and certainly by the nature of the connections (electrotic, excitatory, or inhibitory). Here we investigate only the first two items, namely, the importance of the oscillatory properties of component neurons, and the role of the topology of neural interconnections. Further, we focus only on one critical aspect of the neuron oscillations: is it regular or is it irregular and chaotic. As experiments performed in pyloric neurons show that these oscillations are chaotic, the biological implications of our calculations are focused on the latter.

Further, in the work we present here we use a significantly oversimplified model of the pyloric CPG and of the pyloric chamber. The CPG is “composed” of three neurons only, and the pyloric chamber is comprised of three segments which can expand or contract solely in a radial fashion. We do not pretend this is a realistic, detailed model either of the pyloric CPG with its 14 neurons or of the complex musculature of the pyloric chamber. Further, we neglect known feedback from stretch receptors in the pyloric chamber to CPG neurons. This means our investigation has selected the direct control signals from the CPG to the pyloric chamber as the essential feature which illustrates the selection of the topology of interconnections in the CPG.

Our simplified models are used here to illustrate the core issue: that chaotic component neurons require different connectivity to achieve the same goal as other connections among regular neural components. As experimental observations show the components to be chaotic, the conclusion we draw is quite relevant to biological systems. One could also analyze the network connections through the introduction of lesions or damage to individual synapses. In effect, we do that by allowing our connections to take null as well as positive values, and thus we make a connection with traditional experimental methods in neurophysiology.

The paper is organized as follows. First a description of the two neuron models and the mechanical device are given. Then the simulations are analyzed for both model neurons to yield the results. Finally, a discussion about the interpretation and consequences of the results is given.

2 The periodic model

The periodic spiking-bursting neuron model consists of two compartments: one for the axon (fast generator), and another one for the neuropil and soma (the slow generator). The fast generator provides the spikes with the help of a sodium current $I_{Na}$, a delayed-rectifier potassium current $I_{Kd}$, and a leakage current $I_{Lf}$. We write it as

$$C_m^{axon} \dot{V}_f = -I_{Na} - I_{Kd} - I_{Lf} + I_{V_iV_s},$$

where $C_m^{axon}$ is the axon membrane capacitance, $V_f$ is the membrane potential in the axon, and $V_s$ is the membrane potential of the neuropil and soma. The slow dynamics is provided by

$$C_m^{soma} \dot{V}_s = -I_{Ca} - I_{La} - I_h - I_{K(Ca)}$$

$$- I_{V_iV_s} + I_{Fsyn} + I_{dc},$$

where $C_m^{soma}$ is the soma membrane capacitance, $I_{Ca}$ is the calcium current, $I_{La}$ is the leakage current, $I_h$ is a low
threshold current, $I_{K(Ca)}$ is the potassium calcium dependent current, $I_{dc}$ is the injected current, $I_{v, n}$ is the current connecting both compartments, and $I_{syn}$ is the synaptic current. All these currents are described in detail in (Huerta et al. 2000).

The calcium dynamics are described by the following first-order kinetic equation

$$[Ca] = -z[e_{Ca} - \beta[Ca] + \gamma] ,$$

where the constants $\alpha$, $\beta$, and $\gamma$ are described in Huerta et al. (2000).

The HH model oscillates in a strongly dissipative limit cycle and does not sit in parameter space near a bifurcation point. This turns out to be very important in the results that are explained in the following sections.

3 The chaotic model neuron

The chaotic spiking-bursting model neuron we use in our investigations is a slightly modified version of a HR neuron. It exhibits spiking-bursting behavior as observed in the laboratory, and this alone would not distinguish it from similar behavior of HH-type neuron models. Evidence – peripheral to this study – for the realistic structure of the HR neurons comes from its observed ability to act as a substitute for biological neurons in the lobster pyloric CPG when it is realized in simple analog circuitry and coupled into that biological network (Szűcs et al. 2000). The model has three dynamical variables comprising a fast subset, $x(t)$ and $y(t)$, and a slower variable $z(t)$. $x(t)$ represents the cell’s membrane potential. These dynamical variables satisfy

$$\frac{dx(t)}{dt} = 4y(t) + 1.5x^2(t) - 0.25x^3(t) - 2z(t) + 2e + I_{syn}$$

$$\frac{dy(t)}{dt} = 0.5 - 0.625x^2(t) - y(t)$$

$$\frac{dz(t)}{dt} = -z(t) + 2[x(t) + 3.2] , \quad (1)$$

where $e$ represents an injected DC current, and $\mu$ is the parameter that controls the time constant of the slow variable. The parameters were chosen to place the isolated neurons in the chaotic spiking-bursting regime: $e = 3.281$, $\mu = 0.0021$ (see Szűcs et al. 2000, Wang 1993 and Abarbanel et al. 1996 for the choice of coefficients and parameters).

The main feature of this chaotic neuron is that it is built around a homoclinic loop, which carries the fast oscillations. Motion on the homoclinic loop is structurally unstable, which means that any perturbation close to the homoclinic structure will produce striking differences in its membrane voltage time course: the neuron will either fire another spike or hyperpolarize the membrane (Wang 1993; Abarbanel et al. 1996; Elson et al. 1999). Although they both generate realistic spiking-bursting activity, the dynamical pictures of the chaotic and the regular models are completely different.

In (1) the term $I_{syn}$ represents the postsynaptic current evoked after the stimulation of a chemical graded synapse. In this paper we consider only inhibitory synapses, which is the main kind of interconnection present in the pyloric CPG of the lobster. The synaptic current has been simulated with the traditional description used in the dynamical clamp technique (Sharp et al. 1993) with minor modifications:

$$I_{syn} = -g \cdot r(x_{pre}) \cdot \vartheta(x_{post})$$

where $g$ is the maximal synaptic conductance, and $x_{post}$ is the membrane potential of the postsynaptic neuron. $r(x_{pre})$ is the synaptic activation variable determined from the presynaptic activity by:

$$\frac{dr}{dt} = \frac{r_{\infty}(x_{pre}) - r}{\tau_r}$$

$$r_{\infty}(x_{pre}) = \frac{1 + \tanh((x_{pre} + a)/b)}{2} \quad (2)$$

In our work $A = 1.2$ and $B = 0.9$. $\tau_r$ is the characteristic time constant of the synapse ($\tau_r \approx 100$). $\vartheta(x_{post})$ is a nonlinear function of the membrane potential of the postsynaptic neuron that reduces the strong effect of the large spikes in the HR model. The graded inhibitory connections in the real pyloric CPG are not so sensitive to the spike generation (Marder and Calabrese 1996). We choose

$$\vartheta(x_{post}) = \frac{1}{2}(1 + \tanh((x_{post} + a)/b)) ,$$

and $a = 2.81$ and $b = 0.4$ were chosen so that this function remained linear for the slow oscillations:

$$\left. \frac{d\vartheta(x)}{dx} \right|_{a,b} \approx 1 \quad \text{and} \quad \left. \vartheta(x) \right|_{a,b} \approx 0.$$

4 The models for the CPG and the mechanical device

We have previously built a model CPG that controls a pyloric chamber model (Huerta et al. 2000). The CPG is composed of three neurons with mutual inhibitory coupling, as shown in Fig. 2. The six independent maximal conductances $g_{ij}(i \neq j; i, j = 1, 2, 3)$ are selected as described below. The CPG sends electrical activity to the “muscles” that control the dilation and contraction of the “pyloric chamber” represented here by a simulated mechanical plant. Three neurons are the minimal number of cells that produces a maximization of the average flow of food pumped out of the plant.

The mechanical plant is inspired by the lobster pyloric chamber (Silverston and Moulins 1987). In Fig. 2 we have sketched the model with three joined pipes that can expand or contract radially. The central pipe only dilates and the end pipes only contract; this mimics the behavior of the pyloric chamber of the lobster. The proper dynamical combination of muscle activity influencing the walls of the pipes will lead to movement of shredded food towards the right end of the pyloric chamber.

In our selection procedure for combinations of the $g_{ij}$ values, we set the average transport through the pump in
time $T$ to a set of increasingly larger values and determine which configurations are able to achieve each level of transport. The average throughput over time $T$ is given by

$$\Phi(g_{ij}) = \frac{\rho}{T} \left. \int_{t_0}^{t_0 + T} A(t)v(t) dt \right. ,$$

(3)

where $\rho$ is the density of the material being pumped, $A(t)$ is the cross sectional area of the rightmost pipe section, $v(t)$ is the mean velocity through the rightmost cross section of the plant, and $t_0$ is some starting time. The differential equations determining $A(t)$ and $v(t)$ were derived in Huerta et al. (2000). They come from the Navier-Stokes equations and from mass and energy conservation. We treat the shredded food as homogeneous, incompressible and isothermal, and it moves with a low Reynolds Number which means that the flow is always laminar and all radial velocities in the pipe sections are small. We also assume that no food leaks out during the pumping and that there were no head losses in the joints of the pipes.

Equation 3 is a measure of the amount of food being pumped by the plant because the food needs to be transported from the stomach to the digestive system. This measure misses a feature which for simplicity has not been introduced in the model: that is, the food being filtered by the pylorus. The filtering mechanisms are not known and, therefore, were not included in the model.

In our calculations the mean initial velocities in each section are zero. We choose the $g_{ij}$ values to be 0, 50 nS, or 200 nS in the periodic model, and 0, 0.05, or 0.1 in the chaotic one. Then we evaluate $\Phi(g_{ij})$ for each of these 36 choices. The system is run for a simulated time of 60 s; a transient of $t_0 = 10$ s is eliminated and $\Phi(g_{ij})$ is found by averaging over the last $T = 50$ s (we choose units of milliseconds in the arbitrary time units of the HR model). The system of differential equations is integrated using a Runge-Kutta 6(5) scheme with variable time step and with an absolute error criterion of $10^{-16}$ and a relative error criterion of $10^{-6}$.

In the following section we compare the performance of both regular and chaotic neurons in controlling the pump for the different connection architectures. But before that we want to illustrate with an example the working mechanism of the whole system. Figure 3 shows the membrane potential time series of the CPG neurons, the electrical activity of the muscles, the dynamics of the areas of the pipes, and the food flows for two examples of the connection topologies subjected to study. We can compare how the non-open topology generates a regular rhythm which, in this specific case, is good at producing a positive amount of food flow being pumped out. On the other hand, the open topology produces an output that is near 0. This is one typical simulation out of 15 trials. The final value of the flow is an average of the 15 trials for a given configuration starting with different initial conditions. If the topology solution is not stable the average value of the flow will be lower than that in the stable case.

5 Analysis of solutions

We distinguish these two types of topology:

1. Open topology: in this case there is at least one neuron that receives no connections from the other network elements. This is shown in Fig. 4.

2. Non-open topology: all the neurons in the CPG receive at least one synapse from some other member of the CPG.

In order to quantify the difference between open topologies and the rest we introduce the following definitions. We define the set of solutions with a resulting flow lying in $\Phi_{\text{lower}} \leq \Phi \leq \Phi_{\text{upper}}$ as

$$G(\Phi_{\text{lower}}, \Phi_{\text{upper}}) = \{ (g_{12}, g_{13}, g_{21}, g_{23}, g_{31}, g_{32}); \Phi_{\text{lower}} < \Phi \leq \Phi_{\text{upper}} \}$$

and the subset of open solutions as

$$O(\Phi_{\text{lower}}, \Phi_{\text{upper}}) = \{ (g_{12}, g_{13}, g_{21}, g_{23}, g_{31}, g_{32}); \exists i/j, g_{ij} = 0, \forall j \neq i; \Phi_{\text{lower}} < \Phi \leq \Phi_{\text{upper}} \} .$$

We report the ratio between the number of open solutions $| O(\Phi_{\text{lower}}, \Phi_{\text{upper}}) |$ and the total number of solutions $| G(\Phi_{\text{lower}}, \Phi_{\text{upper}}) |$,

$$\eta(\Phi_{\text{lower}}, \Phi_{\text{upper}}) = \begin{cases} \frac{| O(\Phi_{\text{lower}}, \Phi_{\text{upper}}) |}{| G(\Phi_{\text{lower}}, \Phi_{\text{upper}}) |} & \text{if } | G(\Phi_{\text{lower}}, \Phi_{\text{upper}}) | \neq 0 \\ 0 & \text{if } | G(\Phi_{\text{lower}}, \Phi_{\text{upper}}) | = 0 \end{cases} .$$

(4)
Fig. 3. Membrane potential $V$ time series of the three (chaotic) neurons in the CPG, electrical activity of the muscles $V_n$ that transmits pressure to the pipes, dynamics of the area $A$ of the cross sections of the three pipes, and the net food flow $\Phi$ exiting the artificial pylorus for two examples of the connection topologies subjected to study. Left panel corresponds to an example of non-open topology while the right panel shows the calculations for a test open topology (depicted at top).

Open

![Diagram of open network topology]

Neuron

Fig. 4. Definition of an open network topology: there must be one or more neurons with no connections from other members of the CPG as a quantitative measure of the topology of allowed solutions at a given value of $\Phi$. $|\cdots|$ denotes the cardinality of a set. Since $\left| O(\Phi_{\text{lower}}, \Phi_{\text{upper}}) \right| \leq \left| G(\Phi_{\text{lower}}, \Phi_{\text{upper}}) \right|$, $0 \leq \eta \leq 1$.

We investigated two questions in the calculations reported here:

1. Does the use of chaotic component CPG neurons remove open solutions?
2. Can noise eliminate open solutions when the component CPG neurons are regular oscillators?

In examining the first question we used three different values for each $g_{ij}$ as indicated above, for both the regular neuron model and the chaotic neuron model. The number of configurations was $3^6$. The number of simulation trials for a given configuration pattern was 15 for different random initial conditions. Figure 5 shows a plot of $\eta(\Phi_{\text{lower}}, \Phi_{\text{upper}})$ as defined in 4. We can see that as the flow $\Phi$ increases there are no open topologies of chaotic component neurons that can achieve the flow level. $\Phi$ must be reduced substantially in order to find allowed open topology synaptic connection configurations.

If we build the CPG with regular neurons we see that there are many open topology solutions for high values of $\Phi$. Moreover, $\eta(\Phi)$ is strongly decreasing for the CPG with chaotic neurons. However, the intrinsically regular CPG does not lead to a strong dependence of $\eta$ on the level of the flow. Since isolated neurons in the pyloric CPG appear to oscillate chaotically, a non-open topology of synaptic connections is required to achieve high transport rates for food. Regular neurons can achieve high transport rates in open and non-open configurations, but the pyloric CPG is observed to be non-open. Our calculations provide a suggestive connection between these observations.
To address our second question, white noise $\epsilon(t)$ is introduced in the external injected currents of the Hodgkin-Huxley model (Huerta et al. 2000), so $I(t) = I_0 + \sigma(t)$ where $\sigma$ is the amplitude of the noise. We introduce this type of additive noise for simplicity, because it can be easily integrated (Mannella and Palleschi 1989) since there is no dependence on the other variables of the ordinary differential equations. In Fig. 6 we can see the results of our calculations for eight different values of $\sigma$. For each $\sigma$ value, 20 trials with different initial conditions for a given configuration of $g_{ij}$ values were carried out, and the average of those values was taken as the output of the calculation. The quantity we used to estimate changes as a function of $\sigma$ is

$$
\eta(\sigma) = \begin{cases} 
O_\sigma(\Phi_{th}, \Phi_{\max}) & \text{if } | G_\sigma(\Phi_{th}, \Phi_{\max}) | \neq 0 \\
0 & \text{if } | G_\sigma(\Phi_{th}, \Phi_{\max}) | = 0
\end{cases}
$$

where $\Phi_{\max} = \max_x \{\Phi\}$, and $\Phi_{th}$ is an arbitrary threshold value that determines the existence of good solutions. If a reduction in the number of open configurations is observed, the value $\eta(\sigma)$ must decrease. If our selected configurations are eliminated by noise, then open-topology configurations should disappear and $\eta(\sigma)$ must tend to 0. Otherwise for any value of noise $\eta(\sigma)$ is always greater than 0. In Fig. 6 we can clearly see that for any value of the noise no reduction of the open-topology configurations is observed. Moreover, the quantity $\eta$ approaches 1 for high values of the noise, which answers our question about noise in the positive: open configurations of regular component CPGs are robust against the presence of synaptic noise. The existence of non-open configurations seems to have a different explanation, as we discuss in the next section.

6 Discussion

The results of our model calculations show that – by using periodic neurons – open and non-open connection topologies are possible solutions to the production of a good performance of the mechanical device. However, when chaotic neurons are employed, only non-open connection topologies generate the right output. This leads us to question why nature would select a more complex topology, i.e. non-open, versus open ones. We draw two types of interpretation. One of them does not make use of the fact that some neurons in the CPG are observed to be intrinsically chaotic, and the second does. First, since the real pyloric CPG (like other CPGs) is non-open it is likely that neurons in the CPG are non-periodic. In order to demonstrate this convincingly more test cases in other CPGs are necessary. The second interpretation, which is a conclusion, is driven by the fact that some isolated neurons of the pyloric system of the spiny California lobster are intrinsically non-periodic (Abarbanel et al. 1996; Elson et al. 1999). Since the simulations using a regular model do not rule out non-open topologies, intrinsic chaotic dynamics in the isolated neurons provide a straightforward explanation of the existence of non-open connection topologies in invertebrate CPGs.

Activity of the intact pyloric CPG is mainly regular when observed “in vitro”. It is not a goal of this paper to study how the regularity of the collective patterns influence the functional task of the CPG. However, we want to emphasize that intrinsically chaotic neurons are able to produce regular and stable rhythms when connected within the CPG (see left panel in Fig. 3). It is quite possible that the richer dynamical behavior of the chaotic neurons endows the regular working CPG with additional effective properties (Rabinovich and Abarbanel 1998). The results of the simulations discussed in this paper show that the CPG may require the additional control mechanisms provided by non-open connection topologies as a price for the burden (or the advantage) of having intrinsically chaotic neurons.

The connectivity of neurons in CPGs is probably determined by many developmental and evolutionary factors, and in this paper we have considered an aspect of the required function of a CPG as providing a significant driving force in this topological decision. There are many other invertebrate CPGs, as shown in Fig. 1, and a common thread among these CPGs – whether they are involved in shredding food, as in the gastric CPG of crustacean, feeding, as in the Planorbis and Lymnaea (Staras et al. 1998), or swimming, as in Tritonia – is that the topology of the CPG network is non-open. It would be very interesting to establish whether the connection between network topology, efficiency in biological function, and chaotic neuronal elements holds for these CPG networks as well. We conjecture that the example of lobster pyloric CPG is not special, so that our observations in this example will also appear in other CPG systems.

Since the early papers that showed evidence of chaos in CPG neurons (Mpitsos et al. 1988; Hayashi and Ishizuka 1992) little attention has been given to the role of chaotic neurons in CPGs. It appears that the main reason is that intact CPG networks work in a regular fashion. Indeed, their task is to provide a regular rhythm to the animal so that the muscles that operate in a physical device, such as the pyloric chamber, perform a specific function. Therefore, the interest of modelers was focused mainly on the dynamics of periodic model neurons (Hartline 1979; Ermentrout and Kopell 1986; Terman et al. 1998; Baer et al. 1995; Roberts 1998; Iz- heikevich 1999). In very few cases have modelers tried to understand the potential advantages of using chaotic neurons (Zak 1991; Freeman 1996; Rabinovich and Abarbanel 1998), but typically in more complex systems, not in CPGs. In this work we hope to draw the reader’s attention to an interesting set of roles played by chaotic neurons in CPGs.
As noted in Sect. 1, we are well aware that our work described here is but one avenue of inquiry into the role of chaotic neurons in determining network properties, i.e. the topology of interconnections. We do not address another important issue, namely, the nature of those interconnections. We have greatly simplified our model of the CPG to have only three neurons, rather than the observed 14 in the pyloric CPG, and have made our pyloric chamber “pump” as simple as possible though it is based on physical principles. Both the introduction of other synaptic connections and more complex CPG (including the particularities of each cell type) and “pump” models are called for in further investigations. Our simple models may, however, serve as a baseline for interpreting those more complex calculations.

There are few in vivo studies of the stomatogastric system of the lobster (Clemens et al. 1998a,b). Electromyographic recordings measure the muscle activity, which together with nerve recordings serve to determine the electrical activity of the CPG. In order to test our hypothesis we would need to be able to modulate the connection between the neurons of the pyloric CPG so that the pyloric CPG becomes an open configuration. At the same time, a probe should be introduced into the pylorus so that an indirect measure of the flow can be given (Heinzel et al. 1993). This type of experiment could determine to what extent the open topologies are not adequate to maximize the flow, and how far we stand from reality when we consider a maximization of the flow as the main component of the efficiency function.

Acknowledgements. This work was supported in part by the U.S. Department of Energy, Office of Science, Division of Engineering and Geosciences, under grants DE-FG03-90ER14138 and DE-FG03-96ER14592. Support was also received from the Office of Naval Research under contract ONR/N00014-00-1-0481.

We thank Rob Elson, Allen Silverston, Attila Szecs, Fernando Corbacho, and Manuel Sánchez Montañes for many conversations on the material in this paper.

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