# Real-Time Equivalence of Chemical Reaction Networks and Analog Computers *

Xiang Huang[1][0000−0002−4815−6130], Titus H. Klinge[2][0000−0002−2297−6712], and James I. Lathrop[1]

[1] Iowa State University, Ames, IA 50011, USA {huangx,jil}@iastate.edu
[2] Drake University, Des Moines, IA 50311, USA titus.klinge@drake.edu

**Abstract** This paper investigates the class $\mathbb{R}_{RTCRN}$ of real numbers that are computable in real time by chemical reaction networks (Huang, Klinge, Lathrop, Li, Lutz, 2019), and its relationship to general purpose analog computers. Roughly, $\alpha \in \mathbb{R}_{RTCRN}$ if there is a chemical reaction network (CRN) with integral rate constants and a designated species $X$ such that, when all species concentrations are initialized to zero, $X$ converges to $\alpha$ exponentially quickly. In this paper, we define a similar class $\mathbb{R}_{RTGPAC}$ of real numbers that are computable in real time by general purpose analog computers, and show that $\mathbb{R}_{RTGPAC} = \mathbb{R}_{RTCRN}$ using a construction similar to that of the difference representation introduced by Fages, Le Guludec, Bournez, and Pouly. We prove this equivalence by showing that $\mathbb{R}_{RTCRN}$ is a subfield of $\mathbb{R}$ which solves a previously open problem. We also prove that a CRN with integer initial concentrations can be simulated by a CRN with all zero initial concentrations. Using these results, we give simple and natural constructions showing $e$ and $\pi$ are members of $\mathbb{R}_{RTCRN}$, which was not previously known.

## 1 Introduction

Computing real numbers in real time with a Turing machine was first introduced by Yamada in the 1960s [22] and was later proven to be equivalent to producing the first $n$ bits of the fractional part of the number in $O(n)$-time [15]. It is easy to see that the rational numbers can be computed in real time, but others are not as trivial to compute. Some transcendental numbers are known to be real time computable, such as

$$\lambda = \sum_{n=1}^{\infty} 2^{-n!},$$

which is a Liouville number [18]. Surprisingly, the long standing conjecture by Hartmanis and Stearms that no irrational algebraic number can be computed in real time remains unsolved [18]. If the conjecture is true, it would imply that certain transcendental numbers are easier to compute by a Turing machine than algebraic numbers, which would be surprising indeed.

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Recently, Huang, Klinge, Lathrop, Li, and Lutz defined the class $\mathbb{R}_{RTCRN}$ of real time computable real numbers by chemical reaction networks [19]. They defined a real number $\alpha$ to be in $\mathbb{R}_{RTCRN}$ if there is a CRN with a designated species $X$ that is within $2^{-t}$ of $|\alpha|$ for all $t \geq 1$. Their definition also requires that all rate constants of the CRN be integral, all species concentrations be initialized to zero, and all species concentrations be bounded by some constant $\beta$. This definition is closely related to that of Bournez, Fraigniaud, and Koegler's large population protocols [3], but differs in key technical aspects. A discussion of these differences can be found in [19].

Common variants of the chemical reaction network model assume well-mixed solutions and mass-action kinetics. Small-volume environments such as *in vivo* reaction networks are often modeled stochastically with continuous-time Markov processes, while larger volumes are modeled deterministically with systems of ordinary differential equations[3]. In this paper, we focus on the deterministic mass-action chemical reaction network which is modeled with autonomous polynomial differential equations. Roughly, a chemical reaction network (CRN) is a set of reactions of the form

$$X_1 + X_2 + \cdots + X_n \xrightarrow{k} Y_1 + Y_2 + \cdots + Y_m,$$

where $X_i$ is a *reactant* and $Y_j$ is a *product*. The positive real number $k$ is the *rate constant* of the reaction, and along with the concentrations of the reactants, determines the speed at which the reaction progresses. Although reactions with any number of reactants and products are supported in the model, if they are restricted to exactly two, then stochastic chemical reaction networks are equivalent to population protocols [1].

Recent research has demonstrated that chemical reaction networks are capable of rich computation. They are Turing complete [13], and even weaker variants of the model such as rate-independent environments are still capable of computing a large class of functions [8,9,6]. The reachability problem in CRNs has also recently drawn the interest of computer scientists [5] as well as time complexity issues in the model [11,7]. Chemical reaction networks are also becoming increasingly practical, since they can be compiled into DNA strand displacement systems to be physically implemented [2].

Chemical reaction networks under deterministic mass action semantics are also related to the general purpose analog computer (GPAC), first introduced by Shannon [21]. Shannon's GPAC was inspired by MIT's differential analyzer, a machine designed to solve ordinary differential equations. The model has also recently been refined, and many remarkable results concerning its computational power have been published. The GPAC is Turing complete [17], is equivalent to systems of polynomial differential equations [16], and the class $P$ of languages computable in polynomial time can be characterized with GPACs whose solutions have polynomial arc length [4]. Moreover, Fages, Le Guludec, Bournez,

[3] The stochastic mass action model was proven to be "equivalent in the limit" to the deterministic mass action model as the number of molecules and the volume are scaled to infinity [20].

and Pouly showed in 2017 that CRNs under deterministic mass action semantics can simulate GPACs by encoding each variable as the *difference* of two species concentrations [13].

In this paper, we investigate the relationship between real time computable real numbers by CRNs and general purpose analog computers. We define the class $\mathbb{R}_{RTGPAC}$ of real time computable real numbers by GPACs. Roughly, $\alpha \in \mathbb{R}_{RTGPAC}$ if there exists a polynomial initial value problem (PIVP) with integer coefficients such that, if initialized with all zeros, then all variables are bounded and one of the variables converges to $\alpha$ exponentially quickly. These restrictions are analogous to the definition of $\mathbb{R}_{RTCRN}$ and ensure that the PIVP is finitely specifiable and $\alpha$ is computed in real time. We show that $\mathbb{R}_{RTGPAC} = \mathbb{R}_{RTCRN}$ by proving that $\mathbb{R}_{RTCRN}$ is a subfield of $\mathbb{R}$ and using an extension of the difference representation introduced in [13] that relies on these closure properties. We also show that the constraint of all zero initial conditions can be relaxed to integral initial conditions. With these new theorems, we prove two well-known transcendental numbers $e$ and $\pi$ are members of $\mathbb{R}_{RTCRN}$. The proofs and constructions for these transcendental numbers are short and concise, and demonstrate the power of these theorems for generating and proving real-time CRNs correct.

The rest of this paper is organized as follows. Section 2 introduces relevant definitions and notations used throughout the paper; Section 3 includes the main theorem of the paper, that $\mathbb{R}_{RTGPAC} = \mathbb{R}_{RTCRN}$, along with the proof that $\mathbb{R}_{RTCRN}$ is a field; Section 4 includes proofs that $e$ and $\pi$ are real time computable by chemical reaction networks using the theorems from Section 3; and Section 5 provides some concluding remarks.

## 2 Preliminaries

Chemical reaction networks have been investigated from the perspective of chemistry [12], mathematics [14], and computer science [10], and each field uses slightly different notation. In this paper we use the notion introduced in [19], and thus define a *chemical reaction network* (*CRN*) to be an ordered pair $N = (S, R)$ where $S = \{Y_1, Y_2, \ldots, Y_n\}$ is a finite set of *species* and $R$ is a finite set of *reactions*. A reaction is a triple $\rho = (\mathbf{r}, \mathbf{p}, k)$ where $\mathbf{r}, \mathbf{p} \in \mathbb{N}^n$ are vectors of reactant species and product species, respectively, and $k \in \mathbb{R}_{>0}$ is the rate constant. We use $\mathbf{r}_i$ and $\mathbf{p}_i$ to denote the $i$th component of $\mathbf{r}$ and $\mathbf{p}$, respectively. We call $Y_i \in S$ a *reactant* of $\rho$ if $\mathbf{r}_i > 0$, a *product* of $\rho$ if $\mathbf{p}_i > 0$, and a *catalyst* of $\rho$ if $\mathbf{r}_i = \mathbf{p}_i > 0$.

In this paper, we are concerned with deterministic CRNs under mass action kinetics, and therefore the evolution of a CRN $N = (S, R)$ is governed by a system of real-valued functions $\mathbf{y} = (y_1, \ldots, y_n)$ where $y_i : \mathbb{R}_{\geq 0} \to \mathbb{R}_{\geq 0}$ for all $1 \leq i \leq n$. The value $y_i(t)$ is called the *concentration* of species $Y_i \in S$ at time $t \in [0, \infty)$. According to the law of mass action, the *rate* of a reaction $\rho = (\mathbf{r}, \mathbf{p}, k)$ is proportional to the rate constant $k$ and the concentrations of the reactants $\mathbf{r}$.

Thus, the rate of a reaction $\rho$ at time $t$ is defined as

$$\mathrm{rate}_\rho(t) = k \prod_{Y_i \in S} y_i(t)^{\mathbf{r}_i}. \tag{1}$$

The total rate of change of the concentration $y_i(t)$ of a species $Y_i \in S$ is the sum of the rates of reactions that affect $Y_i$, and thus is governed by the differential equation

$$y_i'(t) = \sum_{(\mathbf{r},\mathbf{p},k)\in R} (\mathbf{p}_i - \mathbf{r}_i) \cdot \mathrm{rate}_\rho(t). \tag{2}$$

This system of ODEs, along with an initial condition $\mathbf{y}(0) \in \mathbb{R}^n_{>0}$, yields a *polynomial initial value problem* (*PIVP*) and has a unique solution $\mathbf{y}(t)$.

For convenience, we allow alternative species names such as $X$ and $Z$ and make use of more intuitive notation for specifying reactions. For example, a reaction $\rho = (\mathbf{r}, \mathbf{p}, k)$ can be written

$$X + Y \xrightarrow{k} X + 2Z, \tag{3}$$

where $\mathbf{r}$ and $\mathbf{p}$ are defined by the complexes $X + Y$ and $X + 2Z$, respectively. Thus $X, Y$ are the reactants of $\rho$, $X, Z$ are the products of $\rho$, and $X$ is a catalyst of $\rho$. If a CRN $N = (S, R)$ consists of only the reaction above, this specifies the system of ODEs

$$\begin{aligned} x'(t) &= 0, \\ y'(t) &= -kx(t)y(t) \\ z'(t) &= 2kx(t)y(t), \end{aligned}$$

where $x(t)$, $y(t)$, and $z(t)$ are the concentrations of the species $X$, $Y$, and $Z$ at time $t$. In this paper we use this intuitive notation whenever possible.

Two CRNs can also naturally be combined into one. Given $N_1 = (S_1, R_1)$ and $N_2 = (S_2, R_2)$, we define the *join* of $N_1$ and $N_2$ to be the CRN

$$N_1 \sqcup N_2 = (S_1 \cup S_2, R_1 \cup R_2). \tag{4}$$

For a CRN $N = (S, R)$ and a species $X \in S$, we say that $(N, X)$ is a *computer* for a real number $\alpha$ if the following three properties hold:

1. **Integral Rate Constants**. For each reaction $\rho = (\mathbf{r}, \mathbf{p}, k) \in R$, the rate constant $k \in \mathbb{Z}_{>0}$ is a positive integer.
2. **Bounded Concentrations**. There is a constant $\beta$ such that, if all species concentrations are initialized to 0, then $y_i(t) \le \beta$ for each species $Y_i \in S$ and for all time $t \ge 0$.
3. **Real-Time Convergence**. If all species in $N$ are initialized to 0 at time 0, then for all $t \ge 1$,
$$|x(t) - |\alpha|| \le 2^{-t}. \tag{5}$$

The real numbers for which there is a computer $(N, X)$ are called *real-time CRN computable*. The set of real-time CRN computable real numbers is denoted by $\mathbb{R}_{RTCRN}$.

The restriction to integral rate constants ensures that the CRN can be specified in finitely many bits. Bounded concentrations imposes a limit on the rate of convergence, which makes the variable $t$ a meaningful measure of time. If concentrations were unbounded, it is possible to compute a real number arbitrarily quickly by catalyzing all reactions with a species whose concentration is unbounded. Bournez, Graça, and Pouly recently showed that the *arc length* of $\mathbf{y}(t)$ is a better time complexity metric [4], and bounded concentrations immediately implies the arc length is linear in $t$, making them equivalent metrics in this case. The real-time convergence requires that $\alpha$ is computed with $\lfloor t \rfloor$ bits of accuracy in $t$ units of time, making it analogous to the definition of real time Turing computation.

The definition of $\mathbb{R}_{RTCRN}$ can also be generalized in the following way. Given two real numbers $\tau, \gamma \in (0, \infty)$, we define $\mathbb{R}_{RTCRN}^{\tau,\gamma}$ in the same way as $\mathbb{R}_{RTCRN}$ except the real-time convergence constraint (5) is replaced with:

$$|x(t) - |\alpha|| \leq e^{-\gamma t}, \tag{6}$$

for all $t \geq \tau$. Proven in [19] but restated here for convenience is the following lemma:

**Lemma 1.** $\mathbb{R}_{RTCRN} = \mathbb{R}_{RTCRN}^{\tau,\gamma}$ *for all* $\tau, \gamma \in (0, \infty)$.

The above lemma shows that the definition of $\mathbb{R}_{RTCRN}$ is robust to linear changes to the real-time convergence rate. Thus, it suffices to show that a CRN computes a real number $\alpha$ exponentially quickly, to prove that $\alpha \in \mathbb{R}_{RTCRN}$ without explicitly showing that $\tau = 1$ and $\gamma = \ln 2$.

## 3 Real-Time Equivalence of CRNs and GPACs

This section is devoted to proving that the class $\mathbb{R}_{RTCRN}$ is equivalent to an analogous class $\mathbb{R}_{RTGPAC}$ of real time computable real numbers by general purpose analog computers. We begin by formally defining $\mathbb{R}_{RTGPAC}$.

For a PIVP $\mathbf{y} = (y_1, y_2, \ldots, y_n)$ satisfying $\mathbf{y}(0) = \mathbf{0}$, we say that $\mathbf{y}$ is an *computer* for a real number $\alpha$ if the following three properties hold:

1. All coefficients of $\mathbf{y}$ are integers,
2. There is a constant $\beta > 0$ such that $|y_i(t)| \leq \beta$ for all $1 \leq i \leq n$ and $t \in [0, \infty)$, and
3. $|y_1(t) - \alpha| \leq 2^{-t}$ for all $t \in [1, \infty)$.

The real numbers for which there is a computer $\mathbf{y}$ are called *real-time GPAC computable*. The set of real-time CRN computable real numbers is denoted by $\mathbb{R}_{RTGPAC}$.

Note that the constraints above mirror the definition of $\mathbb{R}_{RTCRN}$ in Section 2 except for the fact that $y_1(t)$ is converging to $\alpha$ instead of $|\alpha|$. This difference is due to the CRN restriction of species concentrations to be non-negative real numbers whereas the value of a GPAC variable $y_i(t)$ has no such restriction.

**Lemma 2.** $\mathbb{R}_{RTCRN} \subseteq \mathbb{R}_{RTGPAC}$.

*Proof.* Given a computer $(N, Y_1)$ for $\alpha \in \mathbb{R}$, let $\mathbf{y}$ be the PIVP induced by the deterministic semantics of $N$ from equation (2). Note that $(N, Y_1)$ computes $\alpha$ when its species concentrations are initialized to zero, therefore $\mathbf{y}(0) = \mathbf{0}$. The fact that $\mathbf{y}$ is also a computer for $\alpha$ immediately follows from the constraints imposed on $N$ and the fact that if $\alpha < 0$, a multiplying each ODE by $-1$ causes $y_1(t)$ to converge directly to $\alpha$ instead of $|\alpha|$. □

Although the inclusion above is trivial, the fact that $\mathbb{R}_{RTGPAC} \subseteq \mathbb{R}_{RTCRN}$ is not so obvious. This is due to deterministic CRNs inducing PIVPs with restricted forms, namely, the polynomial of each ODE has the structure

$$y'(t) = p(t) - q(t)y(t),$$

where $p$ and $q$ are polynomials over the concentrations of the species. The fact that negative terms in the ODE for $Y$ must depend on its own concentration $y(t)$ makes certain GPAC constructions difficult to implement with CRNs.

The rest of this section is devoted to finishing the proof of the main theorem: $\mathbb{R}_{RTGPAC} = \mathbb{R}_{RTCRN}$. To simplify the proof, we first prove that $\mathbb{R}_{RTCRN}$ is a subfield of $\mathbb{R}$ which solves an open problem stated in [19]. The proofs of closure under addition, multiplication, division, and subtraction rely on certain convergence properties. Thus, we first state and prove two lemmas which demonstrate that certain differential equations immediately yield exponential convergence to a target real number. Then we prove the four closure properties necessary to show that $\mathbb{R}_{RTCRN}$ is a field using these lemmas. Finally, we conclude with the proof of the main theorem that $\mathbb{R}_{RTGPAC} = \mathbb{R}_{RTCRN}$.

**Lemma 3 (Direct Convergence Lemma).** *If $\alpha \in \mathbb{R}$ and $x, f : [0, \infty) \to \mathbb{R}$ are functions that satisfy*

$$x'(t) = f(t) - x(t) \text{ for all } t \in [0, \infty) \tag{7}$$

$$|f(t) - \alpha| \leq e^{-t} \text{ for all } t \in [1, \infty), \tag{8}$$

*then there exist constants $\gamma, \tau \in (0, \infty)$ such that*

$$|x(t) - \alpha| \leq e^{-\gamma t} \text{ for all } t \in [\tau, \infty). \tag{9}$$

*Proof.* Assume the hypothesis. The ODE of equation (7) can be solved directly using the integrating factor method and has a solution of the form

$$x(t) = e^{-t} \int e^t f(t) dt. \tag{10}$$

By equation (8), we know that for all $t \geq 1$,

$$\int e^t f(t) dt \leq \int e^t \left(\alpha + e^{-t}\right) dt = \alpha e^t + t + C_1,$$

for some constant $C_1$. This, along with equation (10), yields

$$x(t) \leq \alpha + e^{-t}\left(t + C_1\right). \tag{11}$$

Using a similar argument, it is easy to show that

$$x(t) \geq \alpha - e^{-t}\left(t + C_2\right) \tag{12}$$

for some constant $C_2$. Choosing $C = \max\{\,0, C_1, C_2\,\}$, it follows from equations (11) and (12) that

$$|x(t) - \alpha| \leq (t + C)e^{-t} \leq e^{-t/2},$$

for all $t \geq \max\{1, 4\log(C+1)\}$. □

**Lemma 4 (Reciprocal Convergence Lemma).** *If $\alpha \in \mathbb{R}_{>0}$ and $x, f : [0,\infty) \to \mathbb{R}$ are continuous functions that satisfy*

$$x'(t) = 1 - f(t) \cdot x(t) \textit{ for all } t \in [0,\infty) \tag{13}$$

$$|f(t) - \alpha| \leq e^{-t} \textit{ for all } t \in [1,\infty), \tag{14}$$

*then there exist constants $\gamma, \tau > 0$ such that*

$$\left| x - \frac{1}{\alpha} \right| \leq e^{-\gamma t} \textit{ for all } t \in [\tau,\infty). \tag{15}$$

*Proof.* Assume the hypothesis. Since $f$ is continuous, its antiderivative exists, so the ODE from equation (13) can be solved directly using the integrating factor method with a solution of the form

$$x(t) = e^{-F(t)} \int_0^t e^{F(s)} ds, \tag{16}$$

where $F(t) = \int_0^t f(s)ds$. If we let $h(t) = f(t) - \alpha$, and let $H(t) = \int_0^t h(s)ds$ be the antiderivative of $h$, then

$$F(t) = \int_0^t (\alpha + h(s))\, ds = \alpha t + H(t).$$

Using this relationship, we can rewrite equation (16) as

$$x(t) = e^{-F(t)} \cdot \frac{1}{\alpha} \int_0^t e^{H(s)} \left(\alpha e^{\alpha s}\right) ds. \tag{17}$$

We can now use integration by parts on the integral of equation (17) with $u(s) = e^{H(s)}$ and $v'(s) = \alpha e^{\alpha s}$ to obtain

$$\begin{aligned}
\int_0^t e^{H(s)} \left(\alpha e^{\alpha s}\right) ds &= \int_0^t u(s)v'(s)ds \\
&= u(s)v(s)\Big|_0^t - \int_0^t v(s)u'(s)ds \\
&= e^{H(t)}e^{\alpha t} - 1 - \int_0^t e^{\alpha s}\left(h(s)e^{H(s)}\right) ds.
\end{aligned}$$

Substituting this into equation (17) and using the fact that $F(t) = \alpha t + H(t)$, we obtain

$$x(t) = e^{-F(t)} \cdot \frac{1}{\alpha}\left(e^{F(t)} - 1 - \int_0^t h(s)e^{F(s)}ds\right),$$

which yields the following bound:

$$\left|x(t) - \frac{1}{\alpha}\right| \leq e^{-F(t)}\left(1 + \int_0^t |h(s)|e^{F(s)}ds\right). \tag{18}$$

It remains to be shown that the right-hand side of equation (18) is bounded by an exponential after some time $\tau$. We begin by showing that $H(t)$ is bounded above and below by the constant $C_1 = \int_0^1 |h(s)|ds + \frac{1}{e}$:

$$|H(t)| \leq \int_0^t |h(s)|ds \leq \int_0^1 |h(s)|ds + \int_1^t e^{-s}ds = C_1 - e^{-t} \leq C_1.$$

It immediately follows that

$$e^{F(t)} = e^{\alpha t + H(t)} \leq C_2 e^{\alpha t}$$
$$e^{-F(t)} = e^{-\alpha t - H(t)} \leq C_2 e^{-\alpha t}$$

where $C_2 = e^{C_1}$. If we define the constant $C_3 = \int_0^1 |h(s)|e^{F(s)}ds$, we can bound the integral of equation (18) with

$$\int_0^t |h(s)|e^{F(s)}ds \leq C_3 + \int_1^t e^{-s}\left(C_2 e^{\alpha s}\right)ds = C_5 + C_4 e^{(\alpha-1)t}$$

where $C_4 = \frac{C_2}{\alpha - 1}$ and $C_5 = C_3 - C_4 e^{\alpha - 1}$. Thus, we can rewrite equation (18):

$$\left|x(t) - \frac{1}{\alpha}\right| \leq C_2 e^{-\alpha t}\left(1 + C_5 + C_4 e^{(\alpha-1)t}\right) = C_6 e^{-\alpha t} + C_7 e^{-t}$$

where $C_6 = C_2(1 + C_5)$ and $C_7 = C_2 C_4$.

It immediately follows that there exist constants $\gamma$ and $\tau$ such that $\left|x(t) - \frac{1}{a}\right|$ is bounded by $e^{-\gamma t}$ for all $t \in [\tau, \infty)$. □

Using Lemmas 3 and 4, we now prove that $\mathbb{R}_{RTCRN}$ is a field. We split the four closure properties into the following four lemmas.

**Lemma 5.** *If $\alpha, \beta \in \mathbb{R}_{RTCRN}$, then $\alpha + \beta \in \mathbb{R}_{RTCRN}$.*

*Proof.* Assume the hypothesis, and let $(N_\alpha, X)$ and $(N_\beta, Y)$ be CRN computers that compute $\alpha$ and $\beta$, respectively. Without loss of generality, we assume that $\alpha, \beta \geq 0$ and that $N_\alpha$ and $N_\beta$ do not share any species.

Now let $Z$ be a new species, and let $N = N_\alpha \sqcup N_\beta \sqcup \widehat{N}$ where $\widehat{N}$ is the CRN defined by the reactions

$$X \xrightarrow{1} X + Z$$
$$Y \xrightarrow{1} Y + Z$$
$$Z \xrightarrow{1} \emptyset.$$

Note that the species in $N_\alpha$ and $N_\beta$ are unaffected by the reactions of $\widehat{N}$, and the ODE for $Z$ is:

$$z'(t) = x(t) + y(t) - z(t). \tag{19}$$

Let $f(t) = x(t)+y(t)$. By Lemma 1, without loss of generality, we can assume that $|f(t) - \alpha - \beta| \leq e^{-t}$ for all $t \geq 1$. Immediately by Lemmas 1 and 3, we conclude that $\alpha + \beta \in \mathbb{R}_{RTCRN}$. □

**Lemma 6.** *If $\alpha, \beta \in \mathbb{R}_{RTCRN}$, then $\alpha\beta \in \mathbb{R}_{RTCRN}$.*

*Proof.* Assume the hypothesis, and let $(N_\alpha, X)$ and $(N_\beta, Y)$ be CRN computers that compute $\alpha$ and $\beta$, respectively Furthermore, we assume that $N_\alpha$ and $N_\beta$ do not share any species. Without loss of generality, we also assume that $\alpha, \beta \geq 0$.

Now let $Z$ be a new species, and let $N = N_\alpha \sqcup N_\beta \sqcup \widehat{N}$ where $\widehat{N}$ is the CRN defined by the reactions

$$X + Y \xrightarrow{1} X + Y + Z$$
$$Z \xrightarrow{1} \emptyset.$$

Note that the species in $N_\alpha$ and $N_\beta$ are unaffected by the reactions of $\widehat{N}$ and yields the following ODE for $Z$:

$$z'(t) = x(t)y(t) - z(t). \tag{20}$$

Let $f(t) = x(t)y(t)$. By Lemma 1, without out loss of generality, we can assume that $|f(t) - \alpha\beta| \leq e^{-t}$ for all $t \geq 1$. Immediately by Lemmas 1 and 3, we conclude that $\alpha\beta \in \mathbb{R}_{RTCRN}$. □

**Lemma 7.** *If $\alpha \in \mathbb{R}_{RTCRN}$ and $\alpha \neq 0$, then $\frac{1}{\alpha} \in \mathbb{R}_{RTCRN}$.*

*Proof.* Assume the hypothesis, and let $(N_\alpha, X)$ be CRN a computer that testifies to this. Without loss of generality, we also assume that $\alpha > 0$.

Now let $Y$ be a new species, and let $N = N_\alpha \sqcup \widehat{N}$ where $\widehat{N}$ is the CRN defined by the reactions

$$\emptyset \xrightarrow{1} Y$$
$$X + Y \xrightarrow{1} X.$$

Note that the species in $N_\alpha$ are unaffected by the reactions of $\widehat{N}$ and yields the following ODE for $Y$:

$$z'(t) = 1 - x(t)y(t). \tag{21}$$

Since $\alpha \in \mathbb{R}_{RTCRN}$, we know that $|f(t) - \alpha| \leq e^{-t}$ for all $t \geq 1$. It follows from Lemmas 1 and 4 that $\frac{1}{\alpha} \in \mathbb{R}_{RTCRN}$. □

**Lemma 8.** *If $\alpha, \beta \in \mathbb{R}_{RTCRN}$, then $\alpha - \beta \in \mathbb{R}_{RTCRN}$.*

*Proof.* Assume the hypothesis, and let $(N_\alpha, X)$ and $(N_\beta, Y)$ be CRN computers that compute $\alpha$ and $\beta$, respectively. Furthermore, we assume that $N_\alpha$ and $N_\beta$ do not share any species. Without loss of generality, we also assume that $\alpha > \beta \geq 0$.

Now let $Z$ be a new species, and let $N = N_\alpha \sqcup N_\beta \sqcup \widehat{N}$ where $\widehat{N}$ is the CRN defined by the reactions

$$\begin{aligned} \emptyset &\xrightarrow{1} Z \\ X + Z &\xrightarrow{1} X \\ Y + Z &\xrightarrow{1} Y + 2Z. \end{aligned}$$

Note that the species in $N_\alpha$ and $N_\beta$ are unaffected by the reactions of $\widehat{N}$ and yields the following ODE for $Z$:

$$z'(t) = 1 - (x(t) - y(t))z(t). \tag{22}$$

Let $f(t) = x(t) - y(t)$. By Lemma 1, without out loss of generality, we can assume that $|f(t) - (\alpha - \beta)| \leq e^{-t}$ for all $t \geq 1$. By Lemmas 1 and 4, we know that $\frac{1}{\alpha-\beta} \in \mathbb{R}_{RTCRN}$. By Lemma 7, we conclude that $\alpha - \beta \in \mathbb{R}_{RTCRN}$. □

**Theorem 1.** $\mathbb{R}_{RTCRN}$ *is a subfield of* $\mathbb{R}$.

*Proof.* This immediately follows from Lemmas 5–8 and the fact that $\mathbb{R}_{RTCRN}$ is non-empty. □

As a consequence of Theorem 1, and the results of [19] we now know that $\mathbb{R}_{RTCRN}$ contains all algebraic numbers and an infinite family of transcendental numbers. However, we have yet to prove that natural transcendentals such as $e$ and $\pi$ are real-time computable by CRNs. These proofs are simplified dramatically using the following theorem which uses a construction similar to [13].

**Theorem 2.** $\mathbb{R}_{RTCRN} = \mathbb{R}_{RTGPAC}$.

*Proof.* We have already shown the forward direction in Lemma 2.

For the backward direction, assume that $0 \neq \alpha \in \mathbb{R}_{RTGPAC}$, and let $\mathbf{y} = (y_1, y_2, \ldots, y_n)$ be the PIVP that testifies to this. Then the individual components of $\mathbf{y}$ obey the ODEs

$$\begin{aligned} y_1' &= p_1(y_1, \ldots, y_n), \\ y_2' &= p_2(y_1, \ldots, y_n), \\ &\vdots \\ y_n' &= p_n(y_1, \ldots, y_n). \end{aligned}$$

For each $1 \leq i \leq n$, we define the variables $\hat{\mathbf{y}} = (z, u_1, v_1, u_2, v_2, \ldots, u_n, v_n)$ as well as the polynomials

$$\hat{p}_i(\hat{\mathbf{y}}) = p_i(u_1 - v_1, u_2 - v_2, \ldots, u_n - v_n),$$

noting that each $\hat{p}_i$ is indeed an integral polynomial over the variables of $\hat{\mathbf{y}}$. For each $1 \leq i \leq n$, we also define the polynomials $\hat{p}_i^+$ and $\hat{p}_i^-$ by the positive and negative terms of $\hat{p}_i$, respectively, whence $\hat{p}_i = \hat{p}_i^+ - \hat{p}_i^-$.

We now define ODEs for each variable $u_i$ and $v_i$ of $\hat{\mathbf{y}}$,

$$u_i' = \hat{p}_i^+ - u_i v_i \left(\hat{p}_i^+ + \hat{p}_i^-\right), \tag{23}$$

$$v_i' = \hat{p}_i^- - u_i v_i \left(\hat{p}_i^+ + \hat{p}_i^-\right), \tag{24}$$

as well as the ODE for the variable $z$

$$z' = 1 - (u_1 - v_1)z. \tag{25}$$

Notice that if $y_i = u_i - v_i$, then

$$u_i' - v_i' = \hat{p}_i^+ - \hat{p}_i^- = \hat{p}_i = p_i = y_i',$$

therefore if $\hat{\mathbf{y}}(0) = \mathbf{0}$, we know that $y_i(t) = u_i(t) - v_i(t)$ for all $t \in [0, \infty)$.

We now prove that every variable of $\hat{\mathbf{y}}$ is bounded from above by some constant. For the sake of contradiction, assume that either $u_i$ or $v_i$ is unbounded. Recall that each variable of $\mathbf{y}$ is bounded by some $\beta > 0$, and therefore $-\beta \leq y_i(t) \leq \beta$ for all $t \in [0, \infty)$. Since $y_i(t) = u_i(t) - v_i(t)$, it follows that *both* $u_i$ and $v_i$ must be unbounded. However, this is a contradiction since $u_i'$ and $v_i'$ each include the negative terms $-u_i v_i \left(\hat{p}_i^+ + \hat{p}_i^-\right)$ which grow faster than their positive terms. Thus, $u_i$ and $v_i$ must both be bounded.

Since each of the ODEs of $\hat{\mathbf{y}}$ can be written in the form $x' = p - qx$ where $p$ and $q$ are polynomials with positive integral coefficients, there exists a CRN $N = (S, R)$ with species $S = \{U_i, V_i \mid 1 \leq i \leq n\} \cup \{Z\}$ that obey these ODEs. Because $y_1 = u_1 - v_1$, this means that $|u_1(t) - v_1(t) - \alpha| \leq 2^{-t}$. By Lemma 4, it immediately follows that $N$ real time computes $\frac{1}{\alpha}$ with species $Z$. Finally, we obtain that $\alpha \in \mathbb{R}_{RTCRN}$ by closure under reciprocal. □

## 4 $e$ and $\pi$ are Real-Time Computable by CRNs

In this section, we will prove that $e$ and $\pi$ are real time computable by CRNs, which was not previously known. However, first we prove a useful theorem that shows that the constraint that the CRN or GPAC must be initialized to all zeros can be relaxed to any integral initial condition. This theorem dramatically simplifies the constructions, since the numbers $e$ and $\pi$ can be naturally computed if a species is initialized to 1.

**Theorem 3.** *If $\alpha \in \mathbb{R}$ and $\mathbf{y} = (y_1, y_2, \ldots, y_n)$, $\mathbf{y}(0) \in \mathbb{Z}^n$ is a PIVP such that*

1. *$|y_i(t)| \leq \beta$ for all $1 \leq i \leq n$ and $t \in [0, \infty)$ for some $\beta > 0$, and*
2. *$|y_1(t) - \alpha| \leq 2^{-t}$ for all $t \in [0, \infty)$,*

*then $\alpha \in \mathbb{R}_{RTGPAC}$.*

*Proof.* Assume the hypothesis. Then there is a polynomial $p_i$ corresponding to each variable $y_i$ of $\mathbf{y}$ such that $y_i' = p_i$. We will now define a related PIVP that when initialized to all zeros computes $\alpha$.

Define the variables $\hat{\mathbf{y}} = (\hat{y}_1, \hat{y}_2, \ldots, \hat{y}_n)$ that obey the ODEs

$$\hat{y}_i' = p_i(\hat{y}_1 + y_1(0), \hat{y}_2 + y_2(0), \ldots, \hat{y}_n + y_n(0)).$$

Since $\mathbf{y}(0) \in \mathbb{Z}^n$, each ODE $\hat{y}_i$ is a polynomial with integral coefficients. We also note that if $\hat{y}_i(t) = y_i(t) - y_i(0)$ for some $t \in [0, \infty)$, then

$$\hat{y}_i'(t) = p_i(y_1(t), y_2(t), \ldots, y_n(t)) = y_i'(t).$$

Thus, if we initialize $\hat{\mathbf{y}}(0) = \mathbf{0}$, it follows that $\hat{y}_i(t) = y_i(t) - y_i(0)$ for all $t \in [0, \infty)$. Since the PIVP $\mathbf{y}$ computes $\alpha$, it follows that the PIVP $\hat{\mathbf{y}}$ computes $\alpha - y_1(0)$, and therefore $\alpha - y_1(0) \in \mathbb{R}_{RTGPAC}$.

Finally, since $y_1(0) \in \mathbb{Z}$, it is also in $\mathbb{R}_{RTGPAC}$, and by closure under addition we conclude that $\alpha \in \mathbb{R}_{RTGPAC}$. □

We now present concise proofs that the $e$ and $\pi$ are members of $\mathbb{R}_{RTCRN}$.

**Theorem 4.** $e \in \mathbb{R}_{RTCRN}$.

*Proof.* By Theorem 3, it suffices to show that there exists a CRN computer with integral initial conditions that computes $e$ exponentially quickly. Consider the CRN defined by

$$X \xrightarrow{1} \emptyset$$
$$X + Y \xrightarrow{1} X$$

along with the initial condition $x(0) = 1$ and $y(0) = 1$. This induces the system of ODES

$$x'(t) = -x(t) \tag{26}$$
$$y'(t) = -x(t)y(t), \tag{27}$$

which is trivial to solve and has solution

$$x(t) = e^{-t}, \qquad y(t) = e^{1-e^{-t}}.$$

It is clear that $y(t)$ exponentially goes to $e$, and thus $e \in \mathbb{R}_{RTCRN}$. □

It is easy to apply the construction of Theorem 3 to the CRN provided in the proof of Theorem 4, and Figure 1 shows the plot of this expanded CRN computing $e$ in this way.

**Theorem 5.** $\pi \in \mathbb{R}_{RTCRN}$.

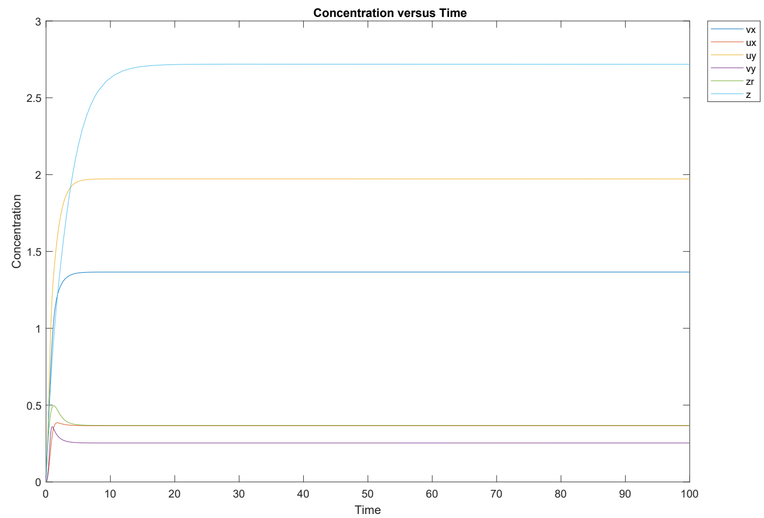


**Figure 1.** MATLAB visualization of computing $e$ from Theorem 4. This plot is of the CRN after applying the construction from Theorem 3 so that all species concentrations are initially zero, and $Z$ is the species converging to $e$.

*Proof.* By Theorem 3, it suffices to show that there exists a CRN computer with integral initial conditions that computes $\pi$ exponentially quickly. Consider the CRN defined by

$$\begin{aligned} W &\xrightarrow{1} \emptyset \\ W + X + Y &\xrightarrow{2} W + Y \\ W + 2X &\xrightarrow{1} W + 2X + Y \\ W + 2Y &\xrightarrow{1} W + Y \\ W + X &\xrightarrow{1} W + X + Z, \end{aligned}$$

with initial condition $w(0) = x(0) = 1$ and $y(0) = z(0) = 0$. It is easy to verify that this CRN induces the following system of ODEs

$$w'(t) = -w(t), \tag{28}$$
$$x'(t) = -2w(t)x(t)y(t), \tag{29}$$
$$y'(t) = w(t)x(t)^2 - w(t)y(t)^2, \tag{30}$$
$$z'(t) = w(t)x(t). \tag{31}$$

By examining equation (28), it is easy to see that $w(t) = e^{-t}$, and by examining equations (29) to (31), we see that we can perform a change of variable from $t$

to $u(t) = \int_0^t w(s)ds = 1 - e^{-t}$ to obtain the equivalent system of ODEs:

$$x'(u) = -2x(u)y(u),$$
$$y'(u) = x(u)^2 - y(u)^2,$$
$$z'(u) = x(u).$$

This system can be solved directly and has solution

$$x(u) = \frac{1}{u^2+1}, \qquad y(u) = \frac{u}{u^2+1}, \qquad z(u) = \arctan(u).$$

Since $\mathbb{R}_{RTCRN}$ is a field, it now suffices to show that $z(t) = z(u(t)) = \arctan(1-e^{-t})$ converges to $\frac{\pi}{4}$ exponentially quickly. Note that Taylor expansion of the function $\arctan(x)$ around 1 gives

$$\arctan(x) = \frac{\pi}{4} + \frac{x-1}{2} - \frac{1}{4}(x-1)^2 + o((x-1)^2).$$

Thus we obtain

$$\arctan(u(t)) - \frac{\pi}{4} = O(u(t) - 1) = O(e^{-t}).$$

Hence $\arctan(1 - e^{-t})$ converges to $\frac{\pi}{4}$ exponentially quickly, and therefore $\pi \in \mathbb{R}_{RTCRN}$. $\square$

It is easy to generate the reactions of the explicit CRN that computes $\pi$ from an all-zero initial condition. The plot of this CRN is provided in Figure 2.

## 5 Conclusion

In this paper, we investigated the relationship of the class $\mathbb{R}_{RTCRN}$ of real time computable real numbers with chemical reaction networks and the class $\mathbb{R}_{RTGPAC}$ of real time computable real numbers with general purpose analog computers. In particular, we proved that $\mathbb{R}_{RTGPAC} = \mathbb{R}_{RTCRN}$ by first solving the previously open problem posed in [19] that $\mathbb{R}_{RTCRN}$ is a field, and then simulating the GPAC with a CRN in a similar way to [13]. In particular, we extend their construction so that our CRN simulation computes the real number $\alpha$ with a *single* species instead of the difference of two species concentrations. We prove this using the reciprocal convergence lemma and the fact that $\mathbb{R}_{RTCRN}$ is closed under reciprocal.

We also used the GPAC equivalence to prove that the restriction to all zero initial conditions is not necessary and can be relaxed to integral initial conditions. This led to concise and natural proofs that $e$ and $\pi$ are in $\mathbb{R}_{RTCRN}$. We should note that applying the constructions in the proofs of Theorems 2 and 3 leads to CRNs with a large number of reactions.

We hope future research will uncover techniques to compute numbers such as $e$ and $\pi$ more efficiently, as well as research that leads to a better understanding of the structure of $\mathbb{R}_{RTCRN}$.

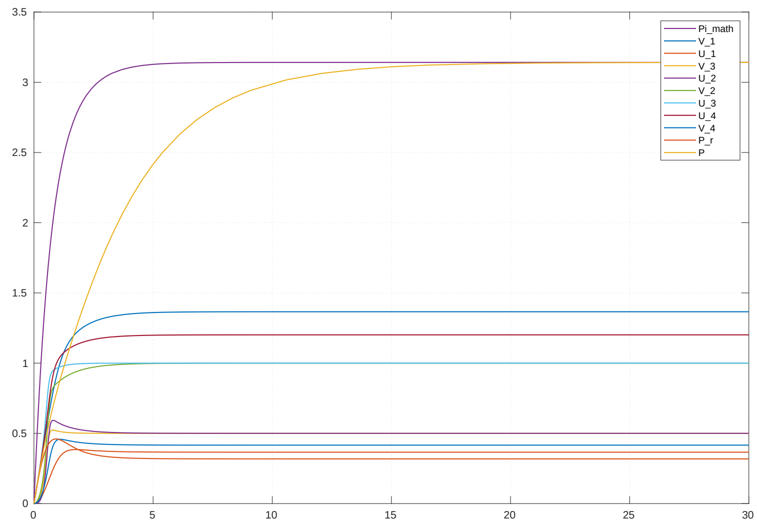


**Figure 2.** MATLAB visualization of computing $\pi$ from Theorem 4. This plot is of the CRN after applying the construction from Theorem 3 so that all species concentrations are initially zero, and $P$ is the species converging to $\pi$.

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