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MATHEMATICAL EXPERIMENTATION IN TIME-LAG MODULATION

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The RAND Corporation
SANTA MONICA • CALIFORNIA

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PREFACE

Part of the RAND research program for the National Institutes of Health consists of basic supporting studies in mathematics. This Memorandum points out some interesting properties of a certain type of differential equation that frequently arises in the course of constructing mathematical models of physical phenomena. This is of importance in connection with the study of more realistic models of chemotherapy, of the type being studied under NIH GM-09608.

SUMMARY

Equations of the form $du/dt = g(u(t),u(h(t)))$ arise in a number of scientific contexts. In this paper, we point out some interesting properties of the solution of

$$u'(t) = -u(t - 1 - k \sin \omega t) + \sin at.$$

These properties were obtained by means of numerical solution.

CONTENTS

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1. INTRODUCTION

In the detailed study of physical phenomena, it is frequently found that the traditional ordinary differential equation must be replaced by the more complicated functional differential equation (see [1,2,3]). In particular, we have met equations of the form

$$\frac{dx}{dt} = g(x(\cdot)), \tag{1.1}$$

where $x(\cdot)$ denotes dependence on the past history of the process over $[0,t]$ in several mathematical models of the heart-lung complex [4]. Examples of equations of this nature are

$$\frac{dx}{dt} = g(x(t),x(t - 1)), \tag{1.2}$$

$$\frac{dx}{dt} = g(x(t),x(h(x,t))),$$

$$\frac{dx}{dt} = g\left(x(t), \int_0^t x(t - s)\varphi(s)ds\right).$$

The solution of these equations not only constitutes an analytic challenge, but also requires a considerable amount of computational care and ingenuity, even with modern computers at our disposal. This is especially so if we wish to calculate the solution over a long time interval. In [5,6,7], we have indicated various techniques that may be used for numerical purposes.

Before tackling large systems of equations of this nature, with unpredictable analytic behavior, it is essential to test our algorithms on simpler equations. Consequently, we felt that it would be interesting to study equations of the form

$$(1.3)\qquad \frac{du}{dt} = -\,u(t-1-k\sin\omega t) + \sin at$$

for different values of a, ω, and k. As we shall see below, some interesting effects are observed. In particular, a variable time—lag produces effects hitherto associated with nonlinearity.

2. A PERTURBATION ANALYSIS

In order to have some idea of what to expect from the calculations, let us apply a perturbation technique to the case $\omega = a = 2\pi$, where $k \ll 1$. The equation is

$$(2.1)\qquad u'(t) = -\,u(t-1-k\sin at) + \sin at,$$

which we write in the form

$$(2.2)\qquad u'(t) = -\,u(t-1) + k\sin at\,u'(t-1) + \sin at + O(k^2).$$

Write

$$(2.3) \qquad u(t) = u_0(t) + ku_1(t) + \cdots,$$

and then substitute and equate coefficients of k to obtain the equations

$$(2.4) \qquad u_0'(t) = -u_0(t-1) + \sin at,$$

$$u_1'(t) = -u_1(t-1) + \sin at u_0'(t-1),$$

$$\vdots$$

At the moment, we are interested in the steady-state periodic solutions. These exist, since all of the roots of the characteristic equation

$$(2.5) \qquad \lambda = -e^{-\lambda}$$

have negative real parts (see [1], Chapter 12). We could use the Laplace transform, but it is simpler to set

$$(2.6) \qquad u_0(t) = c_1 \sin at + c_2 \cos at,$$

and equate coefficients. A direct calculation yields

$$c_1 = \frac{1}{4\pi^2 + 1}, \quad c_2 = -\frac{2\pi}{4\pi^2 + 1} \tag{2.7}$$

(recall that $a = 2\pi$).

The equation for $u_1(t)$ then takes the form

$$u_1'(t) = -u_1(t-1) + \frac{2\pi^2}{1 + 4\pi^2} + p_1(t), \tag{2.8}$$

where $p_1(t)$ is a periodic function with mean value zero.

Hence, $u_1(t)$ has a steady-state form of the following type:

$$u_1(t) = \frac{2\pi^2}{1 + 4\pi^2} + p_2(t), \tag{2.9}$$

where $p_2(t)$ is again a periodic function with mean value of zero.

Since $u(t) = u_0 + ku_1 + \cdots$, we are led to expect a nonzero mean value for $u(t)$, the "output," even though the "input," $\sin 2\pi t$, has mean value of zero. This is a resonance effect, which is not predicted if $\omega \neq a$.

3. NUMERICAL RESULTS

Let us now examine the numerical results, which we obtained via two independent methods. For the values $k = 0.01, 0.05$, the solutions of (2.1), subject to the initial condition $u(t) = 0$, $t < 0$, over the interval $0 \leq t \leq 18$ are shown below.

Calculating the mean values, we find, approximately,

(3.1) $k = 0.01$, 0.0052,

$k = 0.05$, 0.0240.

The term $2\pi^2 k/(1 + 4\pi^2)$ yields

(3.2) $k = 0.01$, 0.0049,

$k = 0.05$, 0.0243.

The perturbation analysis appears valid.

Carrying out the numerical integration for the further values $k = 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9$, we obtain steady-state periodic solutions in all cases, and the mean value as a function of k has the following form (see Fig. 1).

In Fig. 2 and Fig. 3, we show what the solution looks like for $k = 0.1$ and 0.9, respectively.

4. GENERATION OF HARMONICS

One of the functions of nonlinearity is to generate harmonics. This is useful in itself, as for example in frequency multiplication, which is necessary to create different wave forms—as, say, in the multivibrator. It is interesting then to note that a variable periodic time lag has a great capacity for the generation of harmonics. Consider, for example, the following graph (Fig. 4), obtained from the equation

$$(4.1) \qquad u'(t) = -u(t - 1 - k \sin 2\pi t) + \sin \frac{\pi t}{2},$$

$$u(t) = 0, \quad t < 0.$$

$u(t) = -u(t-1-k \sin \omega t) + \sin a t$

$\omega = a = 2\pi$

$u(t) = 0, \; t<0$

k	Machine calculation	$\left(\frac{2\pi^2}{4\pi^2+1}\right) k$
.01	.0052	.0049
05	.0240	.0243

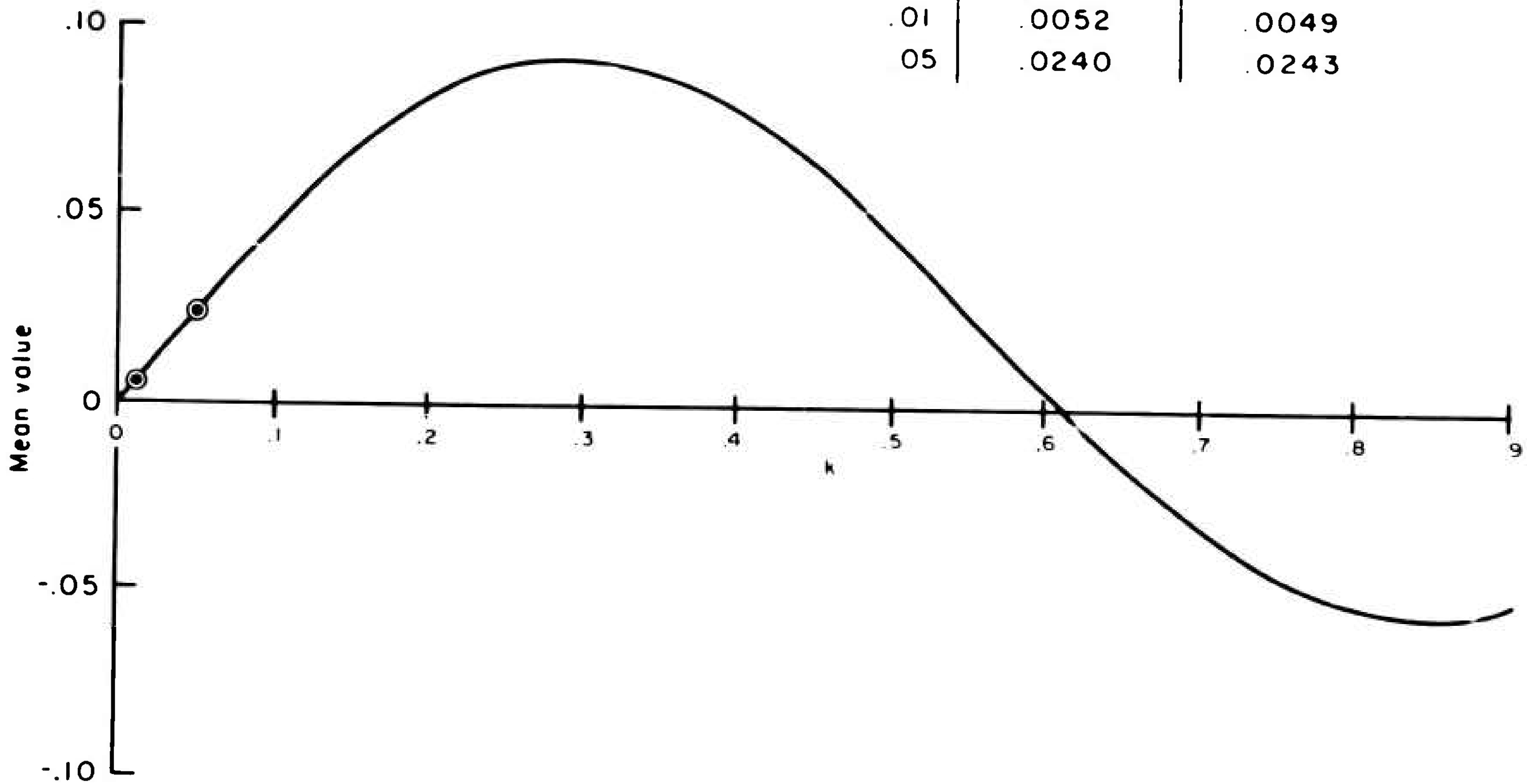
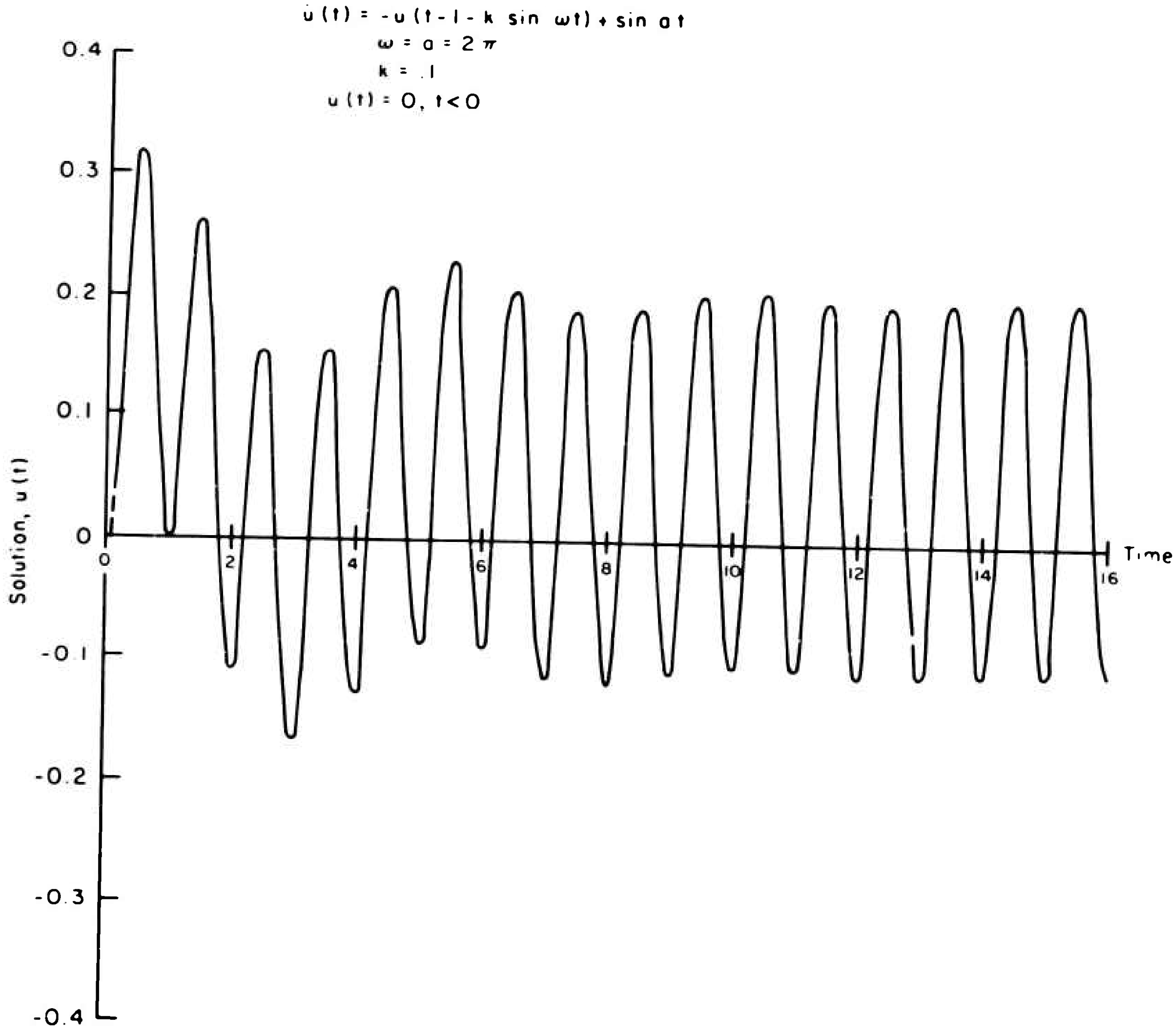


Fig.1



$\dot{u}(t) = -u(t-1-k \sin \omega t) + \sin at$
$\omega = a = 2\pi$
$k = .1$
$u(t) = 0, t<0$
Solution, u (t)
0.4
0.3
0.2
0.1
0
-0.1
-0.2
-0.3
-0.4
0
2
4
6
8
10
12
14
16
Time

Fig.2

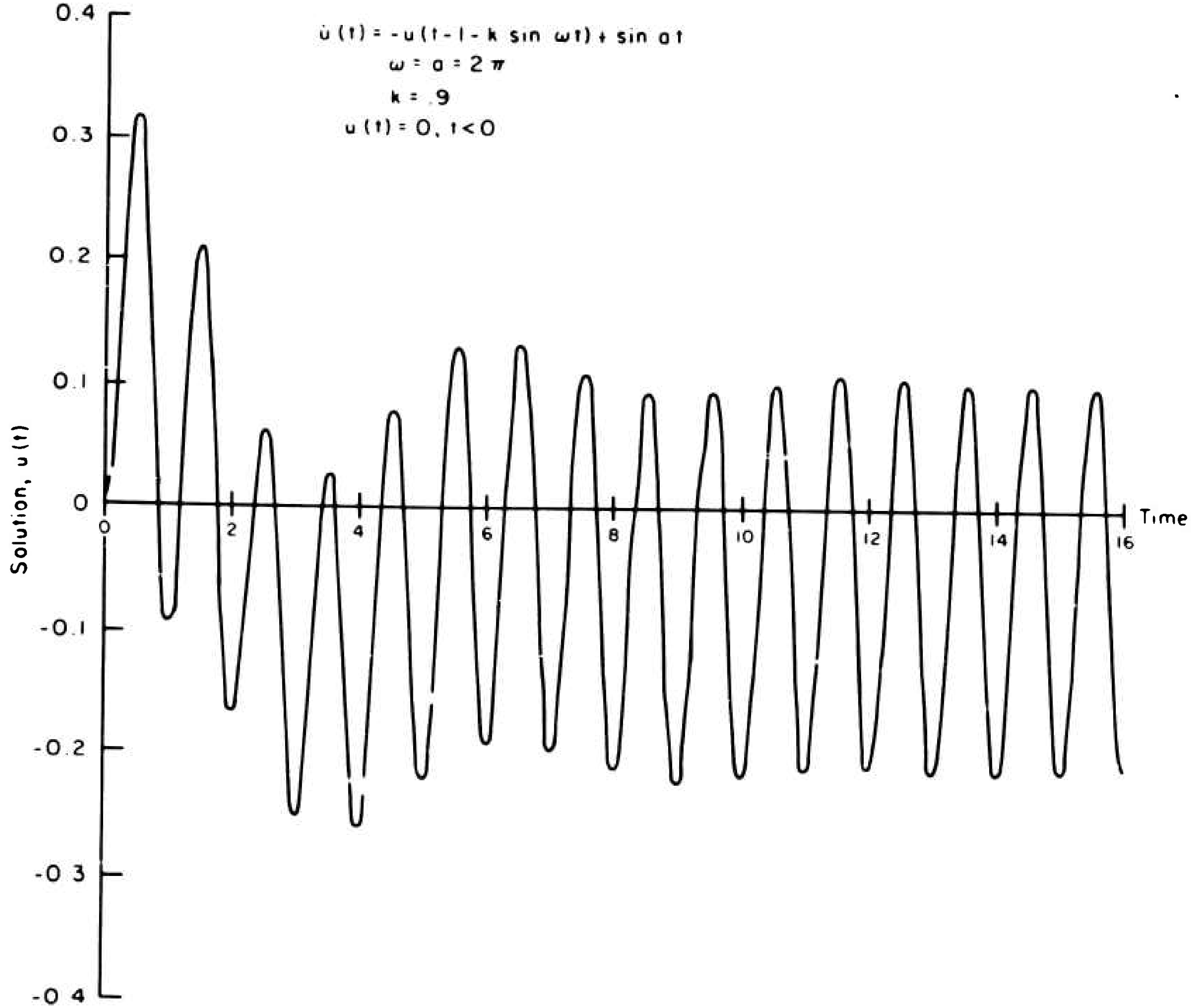

$\dot{u}(t) = -u(t-1-k \sin \omega t) + \sin a t$
$\omega = a = 2\pi$
$k = .9$
$u(t) = 0, t<0$
Solution, u(t)
0.4
0.3
0.2
0.1
0
-0.1
-0.2
-0.3
-0.4
0
2
4
6
8
10
12
14
16
Time

Fig. 3

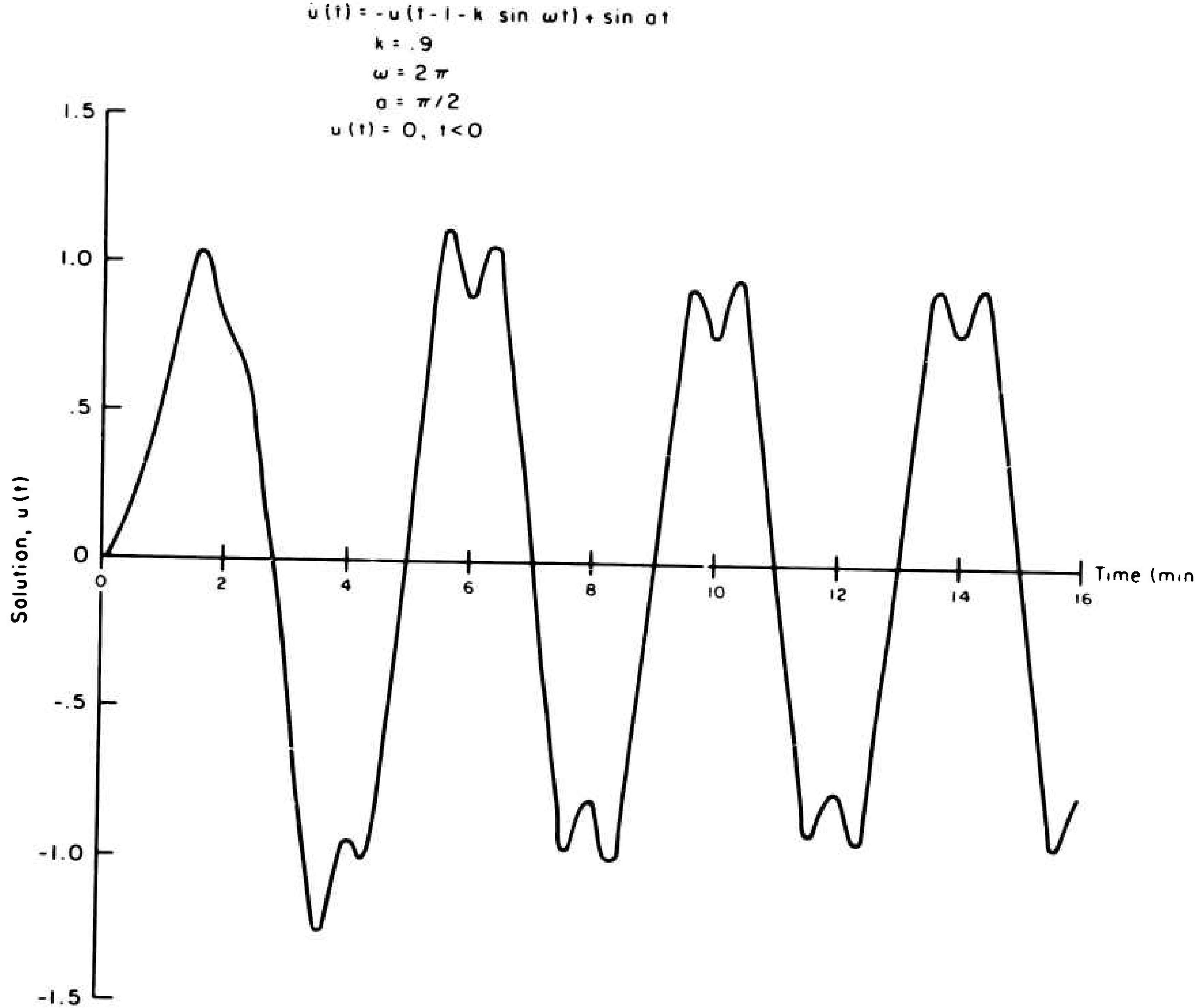

$\dot{u}(t) = -u(t-1-k\ \sin\ \omega t) + \sin\ at$
$k = .9$
$\omega = 2\pi$
$a = \pi/2$
$u(t) = 0,\ t<0$
Solution, u(t)
1.5
1.0
.5
0
-.5
-1.0
-1.5
0
2
4
6
8
10
12
14
16
Time (min)

Fig. 4

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