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Note On a Class of Nonlinear Time Independent Diffusion Equations

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Abstract. *A study of the existence and uniqueness of solutions to two classes of nonlinear time-independent diffusion equations is presented.*

The first non-linear spherically symmetric time-independent diffusion equation is:

$$\frac{1}{r^2}\frac{d}{dr}\left[r^2\frac{d\sigma}{dr}\right] = h(\sigma, r) \quad , \quad R_i \le r \le R_o \tag{1}$$

subject to boundary conditions:

$$\begin{aligned} \sigma(R_i) &= \sigma_i \\ \sigma(R_o) &= \sigma_\infty > \sigma_i \end{aligned} \tag{2}$$

where σ is the oxygen concentration, h an arbitrary oxygen consumption rate, R_i the radius of the necrotic core and R_o the radius of the spherical tumor. Our goal is to determine conditions, on $h(\sigma, r)$ under which a unique solution to problem (1) exists.

The following transformations are used

$$\sigma(r) = \sigma_\infty y(r) \quad , \quad r = x R_o \quad , \quad \eta = \frac{\sigma_i}{\sigma_\infty} \quad , \quad \delta = \frac{R_i}{R_o},$$

$$\ell = \frac{x-\delta}{1-\delta} \quad , \quad y(\ell) = v(\ell) + u(\ell) \quad , \quad u(\ell) = \eta + (1-\eta)\ell,$$

$$\alpha = \frac{\delta}{1-\delta} \quad , \quad \lambda = (1-\delta)^2,$$

$$P(\ell) = (\ell + \alpha)v(\ell) + 2(1-\eta) \quad \text{and} \quad f(y,\ell) = -\frac{R_o^2}{\sigma_\infty}(\ell+\alpha)h(y,x)$$

to yield the system:

$$\frac{dP^2}{d\ell^2} + \lambda f(y,\ell) = 0 \tag{3}$$

$$\text{with} \quad \begin{aligned} P(0) &= 0 \\ P(1) &= 0 \end{aligned}$$

whose solution is given by the integral equation,

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$$P(\ell) = \lambda \int_0^1 K(\ell, \xi, P(\xi)) d\xi \tag{4}$$

where

$$K(\ell, \xi, P(\xi)) = G(\ell, \xi) f(\xi, P(\xi)) \tag{5}$$

and

$$G(\ell, \xi) = \begin{cases} \ell(1-\xi) & , \quad \ell \leq \xi \\ \xi(1-\ell) & , \quad \xi \leq \ell \end{cases} \tag{6}$$

The integral equation (4) has a unique solution $P \epsilon L_2[0,1]$ provided that [1]:
(i) K satisfies a Lipschitz condition,

$$| K(\ell, \xi, z_1) - K(\ell, \xi, z_2) | \leq N(\ell, \xi) \mid z_1 - z_2 \mid \qquad \forall z_1, z_2$$

where N is square integrable with

$$\int_0^1 \int_0^1 \mid N(\ell, \xi) \mid^2 d\ell d\xi = Q^2 < \infty,$$

(ii) $K(\ell, \xi, 0)$ is continuous for ℓ, $\xi \epsilon [0,1]$

(iii) $\mid \lambda \mid < Q^{-1}$
It is assumed that $\left| \dfrac{\partial f}{\partial P} \right| \leq M$ for $0 \leq \ell \leq 1$ and all P.
By the Mean Value Theorem,

$$|K(\ell, \xi, z_1) - K(\ell, \xi, z_2)| = \mid G(\ell, \xi) \mid \left| \frac{\partial f(P, \zeta)}{\partial P} \right| \mid z_1 - z_2 \mid$$

$$\leq M |G(\ell, \xi)| \mid z_1 - z_2 \mid \quad \text{for some} \quad \zeta \epsilon (z_1, \, z_2)$$

Hence, $N(\ell, \xi) = M \mid G(\ell, \xi) \mid$.
It follows that

$$Q^2 = \int_0^1 \int_0^1 M^2 \mid G(\ell, \xi) \mid^2 d\ell d\xi =$$

$$= M^2 \left\{ \int_0^1 \left[\int_0^\xi \mid G(\ell, \xi) \mid^2 d\ell + \int_\xi^1 \mid G(\ell, \xi) \mid^2 d\ell \right] d\xi \right\}$$

$$= M^2 \left\{ \int_0^1 \left[\int_0^\xi \ell^2 (1-\xi)^2 + \int_\xi^1 \xi^2 (1-\ell)^2 d\ell \right] d\xi \right\} = M^2 \frac{1}{90}$$

$$\text{i.e.} \quad Q = \frac{M}{3\sqrt{10}}$$

Therefore, there exists a unique solution to (4) provided

$$M = \sup_P \left| \frac{\partial f}{\partial P} \right| < \frac{3\sqrt{10}}{\lambda} \tag{7}$$

A more complete model from the biological standpoint can be constructed from system (1) by taking into consideration the flux of oxygen at the interfaces R_i and R_o. Thus systeme (1) can be re-examined with the appropriate boundary conditions to get

$$\begin{aligned} &\frac{1}{r^2}\frac{d}{dr}\left[r^2\frac{d\sigma}{dr}\right] = h(\sigma, r) \quad , \quad R_i \le r \le R_o \\ \text{subject to:} \quad &\sigma'(R_i) = 0 \\ &\sigma'(R_o) = m(1-\sigma(R_o)) \end{aligned} \tag{8}$$

where m is a constant representing the permeability of the tissue surface [2], [3].

Again by making the following transformations

$r = R_o x$, $\delta = \frac{R_i}{R_o}$, $\ell = \frac{x-\delta}{1-\delta}$, $\sigma(\ell) = v(\ell) + 1$, $\lambda = (1-\delta)^2$, $\alpha = \dfrac{\delta}{1-\delta}$
$f(\sigma,\ell) = R_o^2(\ell+\alpha)h(\sigma,\ell)$, $\phi(\sigma,\ell) = \lambda f(\sigma,\ell)$

system (8) is reduced to

$$\begin{aligned} &(\ell+\alpha)v''(\ell) + 2v'(\ell) = \phi(\sigma,\ell), \quad 0 \le \ell \le 1 \\ \text{with} \quad &v'(0) = 0 \\ &v'(1) + mv(1) = 0 \end{aligned} \tag{9}$$

with solution given by

$$v(\ell) = \int_0^1 G(\ell,\xi)\phi(\xi)d\xi = \lambda\int_0^1 K(\ell,\xi,v(\xi))d\xi \tag{10}$$

where

$$K(\ell,\xi,v(\xi)) = G(\ell,\xi)f(\xi,v(\xi)) \tag{11}$$

and

$$G(\ell,\xi) = \begin{cases} \frac{m(1+\alpha)(1-\xi)+(\xi+\alpha)}{m(1+\alpha)^2} & , \quad \ell \le \xi \\ (\xi+\alpha)\frac{m(1+\alpha)(1-\ell)+(\ell+\alpha)}{m(1+\alpha)^2(\ell+\alpha)} & , \quad \ell \ge \xi \end{cases} \tag{12}$$

(Conditions under which (10) has a unique solution were stated above).
Once more we assume that $\left|\frac{\partial f}{\partial v}\right| \le M$ for $0 \le \ell \le 1$ and all v, and by the Mean Value Theorem

$$\begin{aligned} \mid K(\ell,\xi,z_1) - K(\ell,\xi,z_2) \mid &= \mid G(\ell,\xi) \mid \left|\frac{\partial f(v,\zeta)}{\partial v}\right| \mid z_1 - z_2 \mid \\ &\le M \mid G(\ell,\xi) \mid \mid z_1 - z_1 \mid \text{ for some } \zeta\epsilon(z_1,z_2) \end{aligned}$$

i.e. $N(\ell,\xi) = M \mid G(\ell,\xi) \mid$

It follows that

$$Q^2 = \int_0^1 \int_0^1 M^2 \mid G(\ell,\xi) \mid^2 d\ell d\xi =$$

$$= M^2 \left\{ \int_0^1 \left[\int_0^\xi \left(\frac{m(1+\alpha)(1-\xi)+(\xi+\alpha)}{m(1+\alpha)^2} \right)^2 d\ell \right.\right.$$

$$\left.\left. + \int_\xi^1 \left((\xi+\alpha) \frac{m(1+\alpha)(1-\ell)+(\ell+\alpha)}{m(1+\alpha)^2(\ell+\alpha)} \right)^2 d\ell \right] d\xi \right\}$$

$$= M^2 \Lambda$$

where

$$\Lambda = \frac{6\alpha^2+2\alpha+9}{12} + \frac{2\beta^2(1+3\ln\beta)}{9} + \frac{2(1-3\ln\beta)(\beta^2+\alpha^3 m)}{9m\beta}$$
$$- \frac{3\alpha^2+\alpha+1}{3\beta} + \frac{\alpha^2(8m^2+3)}{6m^2\beta^3} - \frac{\alpha(1+3\alpha)}{3m\beta^3} + \frac{(4\alpha+1)(2m^2+1)}{12m^2\beta^4}$$
$$+ \frac{6(3\alpha^2+\alpha+1)\ln\beta - 2\alpha^3(1-3\ln\alpha)}{9\,m\beta^2}$$

with $\beta = (1+\alpha)$. (For given m, Λ is a monotone increasing function of α). Thus $Q = M\sqrt{\Lambda}$, and a unique solution to (10) exists provided

$$M = \sup_v \left| \frac{\partial f}{\partial v} \right| < \frac{\sqrt{\Lambda}}{\lambda\Lambda}.$$

It is worth noting that since the metabolic reactions in a cell are catalyzed by enzymes [2], [3], it is possible to express the oxygen consumption rate $h(\sigma, r)$ in (1) and (8) by means of Michaelis-Menten kinetics:

$$h(\sigma, r) = \frac{V\sigma}{\sigma + k_m}$$

where V is the maximum reaction rate, and k_m the Michaelis-Menten constant.

The above conditions are sufficient for uniqueness; whether or not their violation gives rise to solution bifurcation or instability with biologically significant consequences will be explored elsewhere. Note that very general conditions for the existence and uniqueness of solutions have been given in [4]-[6].

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