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Foundations of Algorithms and Computational Techniques in Systems Biology

Adjoint Sensitivity Analysis for Optimization

From: Cao Y, Li ST, Petzold L, Serban R, Adjoint sensitivity analysis or differential-algebraic equations: The adjoint DAE system and its numerical solution, *SIAM Journal on Scientific Computing* **24**: 1076–1089 (2003).

Courtesy of: Joshua F. Apgar, Jared E. Toettcher, Jacob K. White, and Bruce Tidor.

Sensitivity Problem For Dynamic Systems

Dynamic System: $F(\dot{x}, x, u(t,p), p) = 0$

Initial Condition: $x(0) = x_0(p)$

Derived Function: $G(p) = \int_0^T g\left(x(t), p\right) dt$

$$\frac{dG}{dp} = ??$$

Forward Method

Dynamic System: $F(\dot{x}, x, u(t,p), p) = 0$

Initial Condition: $x(0) = x_0(p)$

Derived Function: $G(p) = \int_0^T g\left(x(t), p\right) dt$

$$\frac{dG}{dp} = \int_0^T \frac{\partial g}{\partial x}\frac{dx}{dp} + \frac{\partial g}{\partial p} dt$$

Trick 1: Augment The Problem

$$G(p) = \int_0^T g\left(x(t), p\right) + \lambda^T \underbrace{F(\dot{x}, x, t, p)}_{\text{This is zero}} dt$$

$$\frac{dG}{dp} = \int_0^T \underbrace{g_x \frac{dx}{dp}}_{\text{Hard}} + \underbrace{g_p}_{\text{Easy}} + \lambda^T (\underbrace{F_{\dot{x}} \frac{d\dot{x}}{dp}}_{\text{Hard}} + \underbrace{F_x \frac{dx}{dp}}_{\text{Hard}} + \underbrace{F_p}_{\text{Easy}}) dt$$

Trick 2: Integration By Parts

$$\frac{dG}{dp} = \int_0^T \underbrace{g_x \frac{dx}{dp}}_{\text{Hard}} + \underbrace{g_p}_{\text{Easy}} + \lambda^* (\underbrace{F_{\dot{x}} \frac{d\dot{x}}{dp}}_{\text{Hard}} + \underbrace{F_x \frac{dx}{dp}}_{\text{Hard}} + \underbrace{F_p}_{\text{Easy}}) dt$$

$$\int_0^T \lambda^* F_{\dot{x}} \frac{d\dot{x}}{dp} dt = \left(\lambda^T F_{\dot{x}} \frac{dx}{dp} \right|_0^T - \int_0^T \frac{d}{dt}\left(\lambda^* F_{\dot{x}}\right) \frac{dx}{dp} dt$$

$$\frac{dG}{dp} = \int_0^T \underbrace{\left(g_p + \lambda^* F_p\right)}_{\text{Easy}} + \underbrace{\left(g_x + \lambda^* F_x - \frac{d}{dt}\left(\lambda^* F_{\dot{x}}\right)\right) \frac{dx}{dp}}_{\text{Hard}} dt + \left(\lambda^* F_{\dot{x}} \frac{dx}{dp} \right|_{t=0}^{t=T}$$

Trick 3: Make the hard part 0

$$\frac{dG}{dp} = \int_0^T \underbrace{\left(g_p + \lambda^T F_p\right)}_{\text{Easy}} + \underbrace{\left(g_x - \frac{d}{dt}\left(\lambda^T F_{\dot{x}}\right) + \lambda^T F_x\right) \frac{dx}{dp}}_{\text{Hard}} dt + \left(\lambda^T F_{\dot{x}} \frac{dx}{dp} \right|_{t=0}^{t=T}$$

$$g_x - \frac{d}{dt}\left(\lambda^T F_{\dot{x}}\right) + \lambda^T F_x = 0$$

$$\begin{cases} \frac{d}{dt}\left(\lambda^T F_{\dot{x}}\right) = \lambda^T F_x + g_x \\ \frac{dG}{dp} = \int_0^T \underbrace{\left(g_p + \lambda^T F_p\right)}_{\text{Easy}} dt + \left(\lambda^T F_{\dot{x}} \frac{dx}{dp} \right|_{t=0}^{t=T} \end{cases}$$

Trick 4: For Index 0 and 1 DAEs

The Initial Condition 0 Satisfies The Constraint

$$\lambda^T \frac{\partial F}{\partial \dot{x}}\bigg|_{t=T} = 0$$

For My Problems

$$F = f(x,t,p) - \dot{x} = 0$$

$$\frac{\partial F}{\partial \dot{x}} = \mathbf{I}$$

Putting It All Together

Augmented System

$$\begin{cases} x(0) = x_0(p) \\ \dot{x} = f(x,t,p) \\ \lambda^*(T) = 0 \\ \dot{\lambda}^* = \lambda^* f_x + g_x \end{cases}$$

Sensitivity

$$\frac{dG}{dp} = \underbrace{\lambda^T(0)\frac{dx_0}{dp}}_{\text{Sensitivity to initial conditions}} + \int_0^T g_p + \lambda^T f_p \, dt$$

What Do you Need To Know?

For Your Dynamic System:

$$f(x,t,p) = A_1 x + A_2 x \otimes x + B_1 u + B_2 x \otimes u$$

$$f_x(x,t,p) = A_1 + A_2 (I \otimes x + x \otimes I) + B_2 I \otimes u$$

$$f_p(x,t,p) = A_1^{(p)} x + A_1^{(p)} x \otimes x + B_1^{(p)} u + B_1 u^{(p)} + B_2^{(p)} x \otimes u + B_2 \left(x \otimes I \right) u^p$$

For Your Objective Function:

$$g(x,t,p) = \left(Cx - y\right)^* \left(Cx - y\right)$$

$$g_x(x,t,p) = 2C^* \left(Cx - y\right)$$

$$g_p(x,t,p) = 0$$