Detection of bio-chemical reactions through micro structural interactions

M. A. CHANGIZI, D. E. ROMAN, I. STIHARU
Department of Mechanical and Industrial Engineering, CONCAVE Research Centre, Concordia University, Montreal, QC., Canada

This paper presents a highly accurate and repeatable method to detect micro-level bio-chemical reactions using the interaction between microstructure and the reactant mixed with the chemical marker. The method produces a recognizable deflection signature of the cantilever beam. Such deflections could be very large such that they exceed the linear deflection range. For determination of the large deflections of the tip of cantilever beams, an exact method is proposed. This method is using symmetry groups for finding the closed-form solution which could be applied for any boundary condition case. The open literature provides solution only for two particular loading cases: point force and point moment.

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1. Introduction

Bio chemical reactions could be detected when small amount of bio-specimen and reactant are deposited on a determined portion and interact with a small micro structure. Cantilever beams have been used for this purpose. Although not fully understood, the observed interaction seems to be due to one of the flowing conditions: (1) the local stress-strain gradient due to capillarity forces or even more, due to the molecular binding forces of the free bonds which are re-configured during the reaction; (2) thermal local gradient due to the exothermic/endothermic effect of the bio-chemical reaction. Both conditions have been simulated to evaluate the influence of each and apart from modelling; experiments have been carried out to prove the validity of the concept or evaluate the dynamics of the molecular binding force at the surface of the microstructure.

2. The problem definition and experiments

A small amount of biological mass in aqueous solution and the corresponding reactant in a given proportion are deposited on a cantilever as a droplet. According to [1] experiments recently carried out, when a droplet of enzyme mixed with the marker is set on the micro-cantilever beam it is observed that the mass of the fluid and the superficial tension yield a specific pattern – signature - which is very identifiable for a specific reaction. Although due to gravity, the cantilever is expected to move only downwards, it also curves upwards during the duration of the reaction. The below graph illustrates a generic deflection of beam versus time. As can be seen from Fig-1, as the bio-chemical reactions are slow, the experiment may take up to 1200 sec. During this time the volume of droplet which is in the range of 0.02 µl might evaporate. The present study investigates the phenomena that is at the base of this deflection phenomenon. The sensitivity analysis of the cantilever beam is also carried out. As mentioned above, the explanation of the peculiar signature of the cantilever is unknown but two possible explanations are attempted below. Under the assumption that the upwards deflection might be due to the variation in the superficial tension exerted by the fluid in interaction and by the molecular bonds while re-arranging with the microstructure as well as by a local thermal imbalance due to an endo/exo thermal reaction that could locally occur at the contact between the fluid and the structure, the below formulations are further used to numerically model the phenomena and perform a parametric study vs. the geometry and usage of the sensitive element.

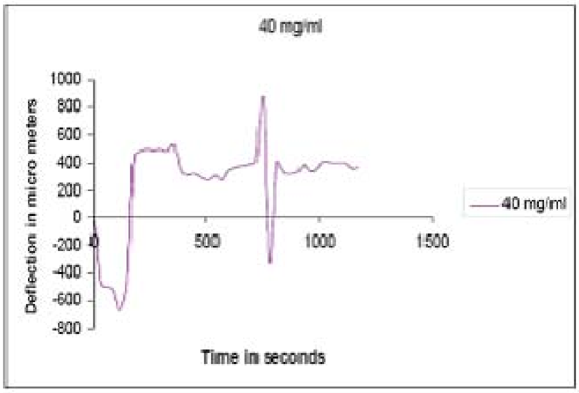

Fig. 1. Defection of micro cantilever beam with respect of time (USPTO patent 20080318242).

3. The superficial tension

For superficial tension analysis, considered that 0.02 µl of semi-sphere shaped fluid is deposited towards the of temperature which in our case could be caused by the endo/exo thermal effect in the droplet due to the bio-chemical reaction. This condition was evaluated by developing an ANSYS model for a micro-cantilever beam. The micro-cantilever beam with length L = 1000 μm, width W = 125μm, thickness T_h = 20 μm was considered. One small part on upper side only of the beam which rectangular area is located at the same position with the position of the droplet is assumed that is heated up by 4°. The results of the analysis are shown on Fig. 5.

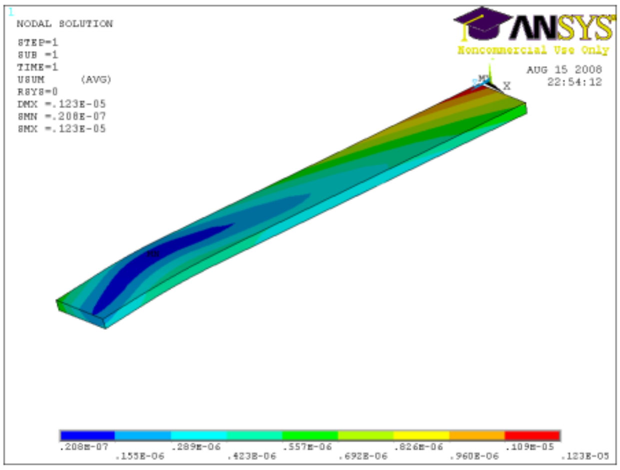

Fig. 5. Deflection of the micro-cantilever beam under temperature difference.

A multi-layered configuration was also analysed. Sensitivity analysis was carried out by considering a 3 layered micro-cantilever beam with length L = 1000 μm configured in the following sequence Al, PVDF, Al. The thicknesses of the layers are as it follows: Al layers: 1 μm, PVDF layer: 18 μm. The width of the beam is W = 125 μm. The materials constants are as it flows: Young modules are $E_{PVDF} = 2e^8$Pa and $E_{AL} = 70e^9$Pa while Poisson ratio nu_{PVDF} = 0.35 and respectively nu_{AL}= 0.3. The temperature difference applied between 750 μm and 900 μm. The temperature difference is 10°C. The figures below show the results:

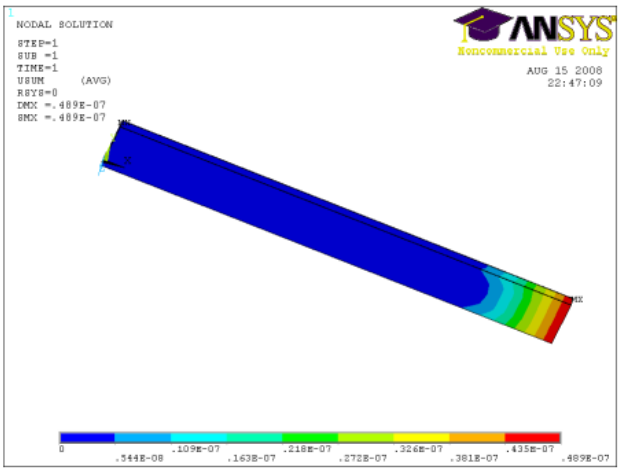

Fig. 6. Deflection of 3 layers micro-cantilever due to temperature gradient.

These analyses show that temperature gradient cannot create significant deflection on the cantilever as the one recorded in the experiment shown in Fig. 1, although the cantilever is long and thin, which are factors that increase their sensitivity. The temperature gradient is considered constant. If the bio-chemical reaction is exothermic, the temperature may be at steady state for the most of the duration of the reaction. Deflection is not necessary due to the mass but to the superficial tension. However, for large deflection the exact determination of the deflection due to any force is still an unsolved problem as the open literature provides results only for two loading cases: point moment and force. The present paper will provide a method for calculating the large deflection in cantilever beams based on symmetry groups.

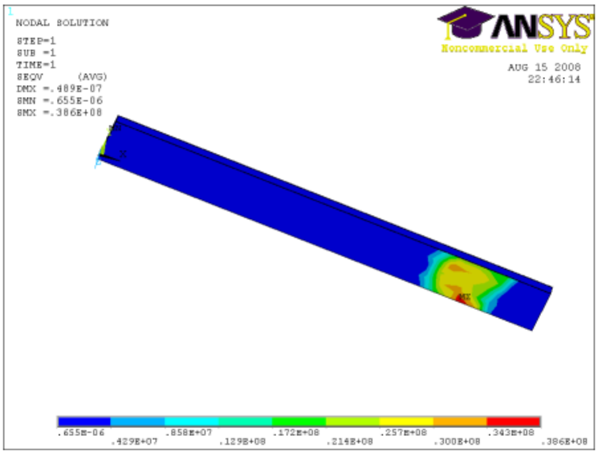

Fig. 7. Stress distribution on a 3 layers micro-cantilever due to temperature gradient.

5. Nonlinear defelction of beams

Deflection of a cantilever can be modeled as [2]:

$$\frac{\frac{d^2y}{dx^2}}{\left(1+\left(\frac{dy}{dx}\right)^2\right)^{\frac{3}{2}}} = \frac{M(x)}{EI} \tag{1}$$

where: $M(x)$ is moment at any section.

E is Young modulus

I is the moment of inertia.

One can show that according [3] infinitesimal transformation is defined as:

$$Xf = \xi(x,y)\frac{\partial f}{\partial x} + \eta(x,y)\frac{\partial f}{\partial y} \tag{2}$$

where:

$$\xi(x,y) = \left.\frac{\partial \phi}{\partial \alpha}\right|_{\alpha=0} \qquad \eta(x,y) = \left.\frac{\partial \psi}{\partial \alpha}\right|_{\alpha=0} \qquad f = f(x,y) \tag{3}$$

where:

$$\frac{du(v)}{dv} = \omega(u,v) = \frac{M(v)}{EI}(1+u(v)^2)^{\frac{3}{2}} \quad (22)$$

Infinitesimal group, ξ and η in (20), must satisfy the below equation:

$$\eta_x + (\eta_y - \xi_x)\omega - \xi_y\omega^2 = \xi\omega_x + \eta\omega_y \quad (23)$$

Substituting (22) in (23) gives:

$$\eta_v + (\eta_u - \xi_v)\frac{M(v)}{EI}(1+u(v)^2)^{\frac{3}{2}} - \xi_u\frac{M(v)^2}{(EI)^2}(1+u(v)^2)^{\frac{3}{2}} = \xi\frac{dM(v)}{dvEI}(1+u(v)^2)^{\frac{3}{2}} + \eta\frac{3M(v)}{EI}u(v)(1+u(v)^2)^{\frac{1}{2}} \quad (24)$$

There is no term of $u(v)(1+u(v)^2)^{\frac{1}{2}}$ in left hand side of equation, so:

$$\eta = 0 \quad (25)$$

Therefore (24) can be written as:

$$-\frac{M(v)}{EI}(\xi_v(1+u(v)^2)^{\frac{3}{2}} + \xi_u\frac{M(v)}{EI}(1+u(v)^2)^3) = \xi\frac{dM(v)}{dvEI}(1+u(v)^2)^{\frac{3}{2}} \quad (26)$$

Comparing the moment in both sides of equation shows that $\xi_u = 0$, so:

$$\xi = \xi(v) \quad (27)$$

By considering (27), equation (26) will simplify to:

$$-\frac{dM(v)}{M(v)dv} = \frac{d\xi(v)}{\xi(v)dv} \quad (28)$$

which its solution is:

$$\xi(v) = \frac{C}{M(v)} \quad (29)$$

where C is constant and can be considered unite. So:

$$\xi(v) = \frac{1}{M(v)} \quad (30)$$

therefore:

$$Xf = \frac{1}{M(v)}\frac{\partial f}{\partial x} \quad (31)$$

Canonical coordinates can be calculated as:

$$r(u,v) = u(v)$$
$$s(u,v) = \int M(v)dv \quad (32)$$

These canonical coordinates satisfy the conditions of (18) and canonical coordinates of ODE can be written as:

$$\frac{ds}{dr} = \frac{EI}{(1+r^2)^{\frac{3}{2}}} \quad (33)$$

where its solution is:

$$s(r) = \frac{rEI}{(1+r^2)^{\frac{1}{2}}} + C_1 \quad (34)$$

or:

$$r = \frac{s(r)+C_1}{\sqrt{-s(r)^2 - 2s(r)C_1 - C_1{}^2 + (EI)^2}} \quad (35)$$

Substituting (32) in (35) gives:

$$u(v) = \frac{\int M(v)dv + C_1}{\sqrt{-(\int M(v)dv)^2 - 2C_1\int M(v)dv - C_1{}^2 + (EI)^2}} \quad (36)$$

Substituting (19) in (36) gives:

$$\frac{dy}{dx} = \frac{\int M(x)dx + C_1}{\sqrt{-(\int M(x)dx)^2 - 2C_1\int M(x)dx - C_1{}^2 + (EI)^2}} \quad (37)$$

So y is:

$$y(x) = \int \frac{\int M(x)dx + C_1}{\sqrt{-(\int M(x)dx)^2 - 2C_1\int M(x)dx - C_1{}^2 + (EI)^2}}dx + C_2 \quad (38)$$

The solution is dependent on two constants which can be established once that two boundary conditions are established.

6. Conclusions

Bio-chemical reactions can be detected through the interaction phenomena at the surface of contact between a fluid-state reactant and marker and a mechanical micro-structure such as a cantilever beam. The motion recorded at the free end of the cantilever beam can be specific to bio-chemical reactions such that ″signature detection″ might be an indicator to a distinct and specific reaction. The upward deflection of the cantilever beams is most likely due to the surface contact phenomena and unlikely due to the thermal effects. The contact phenomena are created by the rearrangement of the free bonds on the large organic molecules while the bio-reaction is occurring.

The deflection of the free end of the beams was analytically calculated for any boundary condition, which