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.

(Received May 4, 2011; accepted August 10, 2011)

Keywords: Bio-chemical reaction, Micro-structure-molecule interaction, Micro-cantilever beam, Deflection signature

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.

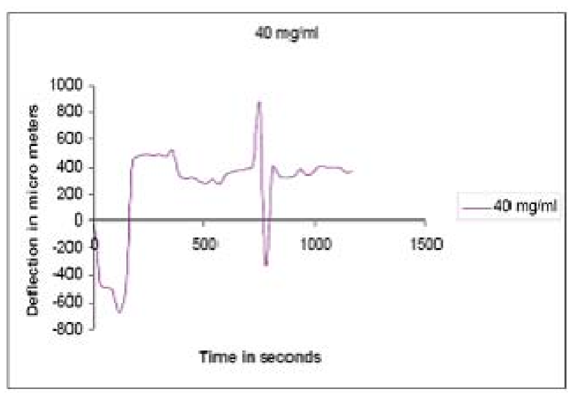

Fig. 1. Defection of micro cantilever beam with respect of time (USPTO patent 20080318242).

3. The surface tension

For superficial tension analysis, considered that 0.02 μl of semi-sphere shaped fluid is deposited towards the free end of the cantilever. Both the mass and the radius of the sphere are thus known. Further, the multi-physics module in ANSYS is used to evaluate both the mass of the droplet and the superficial yield signature as the ones recorded in the experimental analysis. The mass of the droplet is assumed as variable given the fact that some fluid evaporates. Both linear and exponential evaporation laws were assumed. Further, the superficial tension that is assumed to induce the deflection was calculated. The effect of the mass of the fluid is much reduced. The plots in Fig. 2 illustrate the relative superficial tension vs. the superficial tension of water over the duration of the experiment under the assumption of linear and exponential evaporation law vs. time. No significant difference is observed between the two evaporation laws.

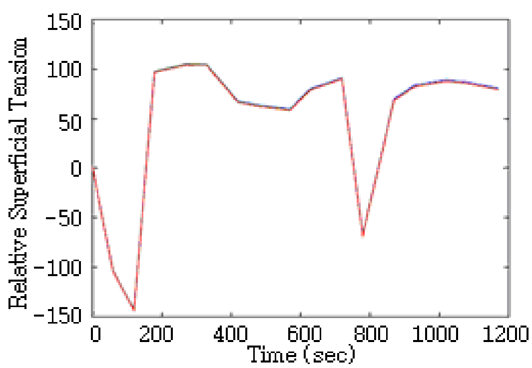

Fig. 2. Relative superficial tension to water versus time based on the signature experiment in Fig. 1.

For the sensitivity analysis two types of assays were carried out. For a known superficial tension for both types of assumed evaporation – linear and exponential and under the assumption of no evaporation at all analysis was carried out. The effect of thickness of the beam in conjunction with the position of droplet was analysed, as one can see in below plots:

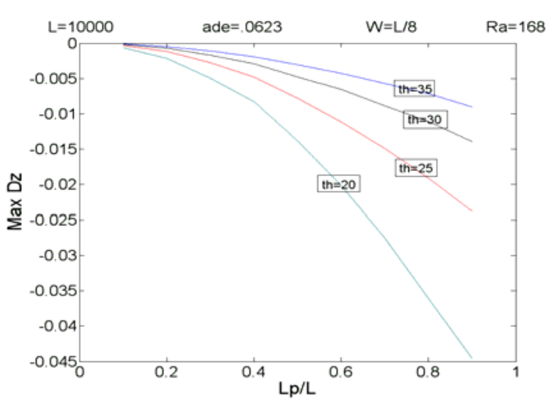

Fig. 3. Thickness and position sensitivity analysis. Superficial tension is .0623 [N/m].

In the above graph the following assumptions and notations are used: the length of the cantilever is assumed L =1,000 μm, W is width of cantilever as L/8, R_a is radius of droplet in μm, L_p is position of the centre of droplet with respect to the fixed end of cantilever, D_z is tip deflection of cantilever in μm while T_h the thickness of cantilever in μm.

From above graph one can notice that:

1) - 60% decreasing in thickness yields an increase of the deflection at the tip of the cantilever by 4.5 times.

2) - Small values of the superficial tension such as the superficial tension of water do not have much effect on micro-cantilever deflection.

The second assay is focused on sensitivity of a superficial tension and the position of the droplet on the deflection of the tip of the cantilever. The length and the width of the cantilever were assumed as in the previous analysis and the thickness was fixed at 20 μm. Assuming variable superficial tension and various positions of the droplet with respect to the fixed end, Fig. 4 was generated.

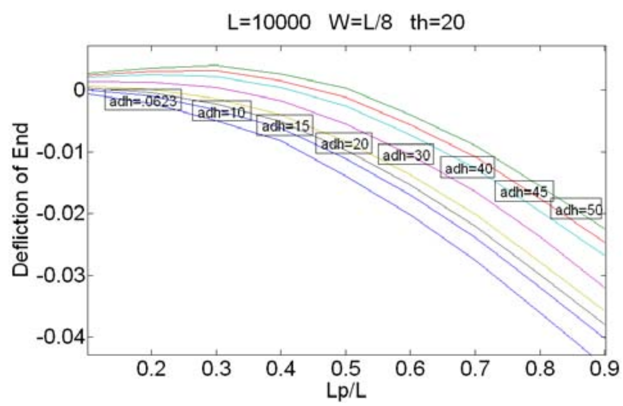

Fig. 4. Sensitivity analysis for variable positions of the droplet and various superficial tension values.

Comparing the above results illustrated in Figs. 3 and 4, one could conclude that:

1) – The increasing in superficial tension will increase the tip deflection when thickness remains constant.

2) – The deflection of the tip of cantilever beam is sensitive to the location of the droplet and the superficial tension. For large superficial tensions of the droplets located in area where $0.4 < \frac{L_p}{L} < 0.5$ yields the maximum pull up values of the cantilever. This effect is more significant when thickness decreases.

3) - When the thickness of the cantilever beam is less than 30 μm and $\frac{W}{L} > 0.1$ the tip of cantilever beam does not pull up in any case.

4) - For any case of location of the droplet > 0.5×L, for any superficial tension and thickness, the tip moves dramatically down.

4. Thermal management of the bio-reaction

The second assumption on the cause that would pull up the tip of a cantilever beam is associated to the local change 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.

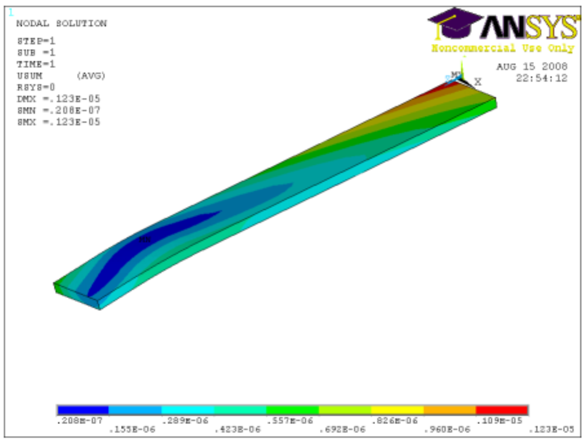

Fig. 5. Deflection of the micro-cantilever beam under temperature difference.

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:

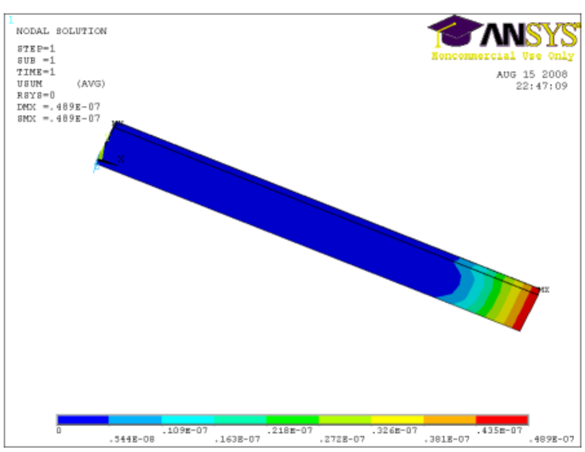

Fig. 6. Deflection of 3 layers micro-cantilever due to temperature gradient.

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.

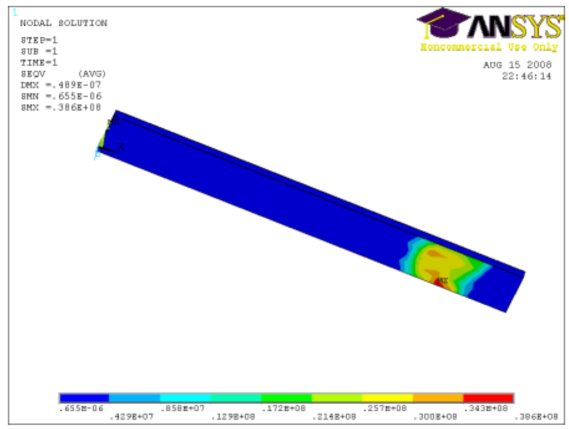

Fig. 7. Stress distribution on a 3 layers micro-cantilever due to temperature gradient.

5. Nonlinear defelction of beams

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

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

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:

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

X is an operator

It can be shown that [3] for a second order differential equation like:

$$\frac{dy^2}{d^2x} = \omega(x, y, \frac{dy}{dx}) \qquad (4)$$

If one is applying an infinitesimal group, ξ and η in (1) must satisfy the below equation:

$$\begin{aligned}&\eta_{xx} + (2\eta_{xy} - \xi_{xx})y' + (\eta_{yy} - 2\xi_{xy})y'^2 - \xi_{yy}y'^3 + (\eta_y - 2\xi_x - 3\xi_y y')\omega = \\ &\xi\omega_x + \eta\omega_y + (\eta_x + (\eta_y - \xi_x)y' - \xi_y y'^2)\omega_{y'}\end{aligned} \qquad (5)$$

By decomposing (5) into a system of PDEs, ξ and η can be calculated. So from (3) the transformation φ and ψ can be calculated. If one consider infinitesimal transformation like:

$$\begin{aligned}\xi &= C_1 + C_2 x + C_3 y \\ \eta &= C_4 + C_5 x + C_6 y\end{aligned} \qquad (6)$$

where: $C_1, C_2, C_3, C_4, C_5, C_6$ are constant numbers. Most of Lie symmetries including rotation, translation and scaling could be found with the above transformations.

For equation (1) ω is defined as:

$$\frac{d^2y}{dx^2} = \omega(x, y, y') = \frac{M(x)}{EI}(1 + (\frac{dy}{dx})^2)^{\frac{3}{2}} \qquad (7)$$

Substitution (5) and (6) in (7) yields:

$$\begin{aligned}&-M(x)C_6 + 2M(x)(\frac{dy}{dx})^2 C_6 + 2M(x)C_2 - M(x)(\frac{dy}{dx})^2 C_2 + 3M(x)\frac{dy}{dx}C_3 + \\ &\frac{dM(x)}{dx}C_1 + \frac{dM(x)}{dx}C_1(\frac{dy}{dx})^2 + \frac{dM(x)}{dx}C_2 x \\ &+ \frac{dM(x)}{dx}C_2 x(\frac{dy}{dx})^2 + \frac{dM(x)}{dx}C_3 y + \\ &\frac{dM(x)}{dx}C_3 y(\frac{dy}{dx})^2 + 3M(x)C_5\frac{dy}{dx} = 0\end{aligned} \qquad (8)$$

This can be written:

$$\begin{aligned}&(-M(x)C_6 + 2M(x)C_2 + \frac{dM(x)}{dx}C_1 + \frac{dM(x)}{dx}C_2 x) + \\ &(2M(x)C_6 - M(x)C_2 + \frac{dM(x)}{dx}C_1 + \frac{dM(x)}{dx}C_2 x + \frac{dM(x)}{dx}C_3 y)(\frac{dy}{dx})^2 + \\ &(3M(x)C_3 + 3M(x)C_5)\frac{dy}{dx} = 0\end{aligned} \qquad (9)$$

All three parentheses must be zero. In first parenthesis coefficients of x and $\frac{dM(x)}{dx}$ are zero:

$$C_2 = 0, C_1 = 0 \qquad (10)$$

therefore:

$$C_6 = 0 \qquad (11)$$

In the second parenthesis coefficient of y must be zero so:

$$C_3 = 0 \qquad (12)$$

In the last parenthesis, in order to have a zero coefficient $C_5 = 0$ must be zero. So only $C_4 \neq 0$, and one can write:

$$\eta = C_4 = 1 \qquad (13)$$

therefore:

$$Xf = \frac{\partial f}{\partial y} \qquad (14)$$

Canonical coordinates can be calculated as [4]:

$$s(r, x) = (\int \frac{dx}{\xi(x, y(r, x))})\Big|_{r=r(x,y)} \qquad (15)$$

where r(x,y) is the solution of:

$$\frac{dy}{dx} = \frac{\eta(x, y)}{\xi(x, y)} \qquad (16)$$

One can show that [5]:

$$\begin{aligned}r(x, y) &= x \\ s(x, y) &= y\end{aligned} \qquad (17)$$

Any canonical coordinates must satisfy the following conditions [5]:

$$\begin{aligned}&\xi(x, y)r_x + \eta(x, y)r_y = 0 \\ &\xi(x, y)s_x + \eta(x, y)s_y = 1 \\ &\begin{vmatrix} r_x & r_y \\ s_x & s_y \end{vmatrix} \neq 0\end{aligned} \qquad (18)$$

It is easy to show that (17) satisfy (18). Reduced form becomes:

$$\begin{aligned}v &= x \\ u(v) &= \frac{dy(x)}{dx}\end{aligned} \qquad (19)$$

Substituting (19) in reducing order form in [3] gives:

$$\frac{du(v)}{dv} = \frac{M(v)}{EI}(1 + u(v)^2)^{\frac{3}{2}} \qquad (20)$$

This is a first order ODE and it is possible to solve it again by Lie symmetry method. It can be shown that [5] for a first order differential equation like:

$$\frac{dy}{dx} = \omega(x, y) \qquad (21)$$

where:

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

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

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

Substituting (22) in (23) gives:

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

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

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

Therefore (24) can be written as:

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

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

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

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

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

which its solution is:

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

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

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

therefore:

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

Canonical coordinates can be calculated as:

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

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

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

where its solution is:

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

or:

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

Substituting (32) in (35) gives:

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

Substituting (19) in (36) gives:

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

So y is:

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

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 method is in detail presented in this paper. It is important to mention that

The large deflection of beams is common to mechanical microstructures such as the cantilever beams used to detect bio-reactions. The large deflection general problem of beams has been so far an unsolved problem for which only solutions such as point moment load and point force both applied at the tip are known from the literature. The analytical solution presented in the paper makes use of Lie symmetry groups.

References

[1] J. Amritsar, I. Stiharu, M. Packirisamy, Proceeding of SPIE, Optical Biochips for Nucleic Acids and Proteins **5969-26**, 2005.

[2] J. M Gere, S. P. Timoshenko, Mechanics of materials, Boston , 1990.

[3] P. J. Olver, Applications of Lie Groups to Differential Equations, Springer, 1993.

[4] G. Emanuel, Solution of ODEs by continuous groups, Chapman, 2001.

[5] H. Stephani, Differential equations, their solution using symmetries, CambridgeUniversity Press 1989.

[6] P. E. Hydon, Symmetry methods for differential equations, Cambridge University press, 2000.

*Corresponding author: mo_chang@encs.concordia.ca