Penetration-force estimation approach for a flexure-jointed micro-injection mechanism with Lorentz force actuation

A. Sura, P. Kuresangsai, M. O. T. Cole*, T. Wongratanaphisan, and P. Puangmali

Department of Mechanical Engineering Faculty of Engineering, Chiang Mai University, Chiang Mai 50200, Thailand

* Corresponding Author: motcole@dome.eng.ac.th

Abstract
This paper presents a novel linear-motion compliant mechanism with Lorentz force actuation and integrated force-sensing capability for automated cell micro-injection. A model-based force estimation approach is introduced such that no force sensor is required. Model identification is undertaken by applying a sinusoidal actuation signal while the mechanism contacts with objects of known stiffness. Displacement data is then used to calculate model coefficients via a least-squares optimization. By using an observer-based state estimation scheme with actuation and displacement signals as inputs, force sensing accuracy within 70 μN RMS error could be achieved within a sensing range of 0 – 5 mN. This sensing capability confirms the suitability of the system for penetration force measurement in certain cases of cell micro-injection.

Keywords: Cell injection, Disturbance observer, Force sensing, Compliant mechanism

1. Introduction
The has been considerable research interest on micromanipulation systems for biological and medical procedures such as Intracytoplasmic Sperm Injection (ICSI) and In Vitro Fertilization (IVF) [1]. Manual ICSI requires skilled operators to control the manipulator and is very time-consuming. Therefore, methodologies for automating this process are currently under development [2], [3]. It is generally recognized that information about the forces acting on the micropipette can be used to better control the injection process, particularly to avoid excessive speed or force that would cause the pressure within the cell to increase and negatively affect or damage the cell [4].

To obtain real-time measurements of penetration force, Wei and Xu [5] developed a force sensor based on a parallel flexure mechanism with piezoelectric polymer (PVDF) film. The device was applied in crab egg micro-injection and could successfully measure penetration forces of approximately 30 mN. A commercial PVDF force sensor was used by Huang et al. [2] for combined position/force control in a novel batch micro-injection system. Sun et al. [6] used a capacitive force sensor with comb drives for micro-injection of mouse oocytes. This type of MEMs sensor is currently costly and extremely fragile, which makes it less practical for general use. Other micro-force sensing methods include the use of piezo-resistive elements, strain gauges, and optical methods to measure strain [7], [8]. With any type of force sensor, it is a challenge to integrate the sensing device within the position control system for the cell or micropipette, while maintaining accuracy, cost-effectiveness and ease of use in practice [3].
This current study considers an alternative approach to force-sensing in microinjection where interaction forces are estimated from knowledge of actuation force and measured displacement of the micropipette. To successfully implement this technique, several important system features are adopted:

1) Flexure-jointed mechanism for high fidelity and transparency of force transmission.
2) Voice coil actuation to achieve low-stiffness and high-fidelity motion.
3) Model-based micro-force estimation scheme using precise position measurements.

This paper also focuses on model calibration and initial investigations on suitable force estimation algorithms. The main results concern the influence of mechanical stiffness and issue of noise contamination.

2. System description

A motion control system for cell injection procedures has been created based on a multi-link compliant mechanism, as shown in Figure 1. In this mechanism, two flexure-jointed linkages are used to support a linear stage with a micropipette (see also Figure 1a). The mechanism is driven by rotatory voice coil actuators to produce rectilinear motion of the stage. Displacement of the stage is measured by a linear optical encoder (resolution 0.2 \( \mu \)m). The actuators are powered by linear drives (Sprint Electric 200XLV) with current range \( \pm 0.2 \) A and current control resolution of 24 \( \mu \)A. A manually operated XYZ stage is used to position the target object for interaction with the micropipette. The mechanism is manufactured by fused deposition modelling (3-D printing) with ABS filament. Key properties of the system are shown in Table 1, while further details on the mechanism design can be found in [9].

The flexure joints allow smooth and precise motion of the stage with low friction. In this present study, the mechanism was controlled in open-loop without feedback. Signal processing was implemented in discrete time with a sampling period of 1 ms. The intrinsic stiffness of the mechanism due to joint stiffness (as measured at the output stage) is approximately 650 N/m. To examine the effect of the mechanism stiffness on force measurements, a stiffness reduction device was attached to the linear stage. This device is a negative stiffness mechanism based on two parallel beams with compressive loading set by a preload spring. The negative stiffness property (which can be determined according to buckling theory [10]) is used to partially cancel the positive stiffness of the linear stage mechanism.

### Table 1. System key properties

| Property                              | Value             | Units |
|---------------------------------------|-------------------|-------|
| Link lengths \((l_1, l_2, l_3, l_4, l_5)\) | (40,20,120,50,120) | mm    |
| Position measurement resolution       | \(2 \times 10^{-4}\) | mm    |
| Current control resolution            | \(2.5 \times 10^{-2}\) | mA    |
| Linear motion range (maximum)         | \(\pm 3\)          | mm    |

Figure 1. Motion system for automated cell micro-injection: (a) schematic diagram of flexure-jointed mechanism (b) experimental setup for calibration and testing.
3. Mechanism model and error analysis

As a basis for force-sensing and system analysis, the mechanism can be represented by a linear dynamic model with a single positional degree of freedom, according to

\[ k_x x + c_x \dot{x} + m_x \ddot{x} = k_i i + f. \]  

(1)

Here, \( x \) is the displacement of the end link from the equilibrium position, \( f \) is the interaction force and \( i \) is the actuator coil current (see Figure 1). The constant coefficients \( k_x, c_x \) and \( m_x \) are the effective stiffness, damping and mass of the mechanism while \( k_i \) is the force/current coefficient for the actuators.

Under static conditions (with \( \dot{x} = \ddot{x} = 0 \)), Equation (1) simplifies to \( f = k_x x - k_i i \). Hence, the absolute error \( \Delta f \) for static force sensing, based on knowledge of \( x \) and \( i \), may be obtained as

\[ \Delta f = k_x \Delta x + k_i \Delta i, \]

(2)

where \( \Delta x \) and \( \Delta i \) are the absolute error/resolution for displacement measurement and actuator current, respectively. For a well-designed system, the dependency of \( \Delta f \) on the input/output should be balanced so that \( k_x \Delta x \approx k_i \Delta i \). For example, if \( k_x \Delta x > k_i \Delta i \) then reducing the mechanism stiffness will improve force-sensing precision by lowering \( k_x \). However, if the stiffness is too low, the mechanism will be prone to positional drift and instability. In this study, the negative stiffness device is introduced so that the effect of stiffness reduction can be investigated in a systematic manner. Although force-sensing accuracy will be affected by other error sources, such as noise and vibration, as well as model error, the underlying limits of precision, as given by Equation (2), must still be examined.

4. Model calibration

4.1 Method

To perform model calibration, a sinusoidal actuation signal with frequency \( \omega \) is applied to excite the system. Under steady-state conditions, the measured input-output data can be expressed as

\[ i(t) = A_i \cos \omega t + B_i \sin \omega t + C_i, \quad x(t) = A_x \cos \omega t + B_x \sin \omega t + C_x, \]  

(3)

where the coefficients \( A_{i,x}, B_{i,x} \) and \( C_{i,x} \) are to be determined. By defining the sampled input-output data in vector form \( \mathbf{i} = [i(t_1) ... i(t_n)]^T, \quad \mathbf{x} = [x(t_1) ... x(t_n)]^T \), the errors in Equations (3) are expressed as

\[ \mathbf{e_i} = \mathbf{R} \mathbf{A_i} - \mathbf{i}, \quad \mathbf{e_x} = \mathbf{R} \mathbf{A_x} - \mathbf{x}, \]  

(4)

where \( \mathbf{R} = \begin{bmatrix} \cos \omega t_1 & \sin \omega t_1 & 1 \\ \cos \omega t_2 & \sin \omega t_2 & 1 \\ \vdots & \vdots & \vdots \\ \cos \omega t_n & \sin \omega t_n & 1 \end{bmatrix} \).

Solutions that minimize \( \mathbf{e_i} \) and \( \mathbf{e_x} \) in a sum-of-squares sense can be computed as

\[ \begin{bmatrix} A_i \\ B_i \\ C_i \end{bmatrix} = (\mathbf{R}^T \mathbf{R})^{-1} \mathbf{R}^T \mathbf{i}, \quad \begin{bmatrix} A_x \\ B_x \\ C_x \end{bmatrix} = (\mathbf{R}^T \mathbf{R})^{-1} \mathbf{R}^T \mathbf{x}. \]

(5)

To determine the model coefficient values, a series of tests are performed where the needle contacts with a linearly elastic object of known stiffness \( k_b \). In this case, \( f = k_b x + F_0 \) and so, from Equation (1), the input-output data is related by

\[ k_b x + F_0 = k_x x + c_x \dot{x} + m_x \ddot{x} - k_i i. \]

(6)

Substituting for \( x \) and \( i \) using equation (3) and matching terms in \( \cos \omega t \) and \( \sin \omega t \) gives

\[ \begin{bmatrix} A_x k_b \\ B_x k_b \end{bmatrix} = \begin{bmatrix} A_x \\ B_x \end{bmatrix} k_x + \begin{bmatrix} \omega B_x \\ -\omega A_x \end{bmatrix} c_x + \begin{bmatrix} -\omega^2 A_x \\ -\omega^2 B_x \end{bmatrix} m_x - \begin{bmatrix} A_i \\ B_i \end{bmatrix} k_i. \]

(7)

When using low-frequency excitation (small \( \omega \)), inertia effects may be neglected so that the \( m_x = 0 \).
A number ($M$) of excitation tests are performed involving interaction with different objects of known stiffness: $k_b = k_b^1, k_b^2, ..., k_b^M$. For each experiment, the coefficients for the input-output data are computed using Equation (5). These are used in Equation (7) and combined in matrix form

$$f_M - G_M \begin{bmatrix} k_x \\ c_x \\ k_i \end{bmatrix} = 0,$$

where

$$G_M = \begin{bmatrix} A_1^k & \omega B_1^c & -A_1^i \\ B_1^x & -\omega A_1^x & -B_1^i \\ \vdots & \vdots & \vdots \\ A_M^k & \omega B_M^c & -A_M^i \\ B_M^x & -\omega A_M^x & -B_M^i \end{bmatrix}$$

As, in general, this equation is overdetermined and cannot be exactly satisfied, the error is defined as

$$e_F = f_M - G_M \begin{bmatrix} k_x \\ c_x \\ k_i \end{bmatrix}^T.$$

Minimizing $e_F$ in a sum-of-squares sense gives the following solution for the model coefficients:

$$\begin{bmatrix} k_x \\ c_x \\ k_i \end{bmatrix} = (G_M^T G_M)^{-1} G_M^T f_M.$$

Note that a minimum of two sets of data (with two different values of $k_b$) is required so that $\text{rank}(G_M) \geq 3$ and the matrix $G_M^T G_M$ is nonsingular.

### Table 2. Identified model parameters for different stiffness-reduction settings.

| Case | Preload (no. of turns) | $k_x$ (N/m) | $c_x$ (Ns/m) | $k_i$ (N/A) | $\omega_d$ (rad/s) | $m_x$ (kg) |
|------|------------------------|-------------|--------------|-------------|-----------------|-------------|
| A    | 0                      | 656.7       | 77.8         | 0.8196      | 110.4250        | 0.0539      |
| B    | 2                      | 329.4       | 50.5         | 0.7625      | 81.9724         | 0.0490      |
| C    | 4                      | 104.4       | 36.7         | 0.734       | 44.8479         | 0.0400      |

### 4.2 Results

To perform the model identification, a thin steel beam (thickness 0.2 mm, effective length 55 mm and width 12.7 mm) was clamped at the one end, while the other (free) end had continuous contact with the needle (see also Figure 1). The beam stiffness, calculated with Euler-Bernoulli theory, was $k_b = 33.4$ N/m. Displacement-current data was collected during steady motion of the mechanism under sinusoidal excitation. This was done both with and without contact of the needle with the beam. A typical data set is also illustrated in Figure 2.
Table 2 presents the identified model coefficients, calculated by the method used in this study (see Section 4.1) and for cases with different preload settings for the negative stiffness mechanism. The effective stiffness of the mechanism $k_x$ is reduced as the preload on the negative stiffness mechanism is increased. It is observed that the effective damping coefficient $c_x$ also decreases as the stiffness is lowered. Some variation in $k_i$ is also observed, which is believed to be due to nonlinear effects impacting on the force transmission. Effective mass values $m_x$ were also calculated using step response data (see example in Figure 3). By measuring the frequency of oscillation $\omega_d$ the mass value could be estimated as $m_x = k_x / \omega_d^2$, in accordance with the model defined by Equation (1).

5. Estimation of interaction forces

5.1 Inverse model approach
A simple method to estimate the object interaction force is based directly on Equation (1). If the mass effects are neglected, the force estimate can be calculated from $i$ and $x$ according to

$$\tilde{f} = k_x x + c_x v - k_i i,$$

(11)

where $v(t)$ is an estimate of the end-link velocity $\dot{x}(t)$. This may be obtained using a filtered-derivative operation (with cut-off frequency $\omega_c$), which has the state equation $\dot{v} = -\omega_c z + \omega_c x$. The force estimation scheme is implemented by combining this with Equation (11):

$$\dot{z} = -\omega_c z + \omega_c x,$$

(12)

$$\tilde{f} = (k_x - \omega_c c_x)x - \omega_c c_x z - k_i i.$$

(13)

Although this approach is simple to design and implement, it does not provide an optimal estimate of $f$ when external disturbances and noise act on the system during operation.

5.2 Disturbance observer approach
An optimal estimation of $f$ should take account of system perturbations, such as noise and vibration excitation (e.g., due to ground vibration and acoustic noise). For stochastic disturbances, it is appropriate to consider an optimal state estimator based on a model of the system in the form

$$\frac{d}{dt} \begin{bmatrix} x \\ \dot{x} \end{bmatrix} = \begin{bmatrix} -\frac{k_x}{m_x} & -\frac{c_x}{m_x} \\ \frac{k_i}{m_x} & \frac{1}{m_x} \end{bmatrix} \begin{bmatrix} x \\ \dot{x} \end{bmatrix} + \begin{bmatrix} 0 \\ \frac{1}{m_x} \end{bmatrix} f + \begin{bmatrix} 0 \\ \frac{1}{m_x} \end{bmatrix} d,$$

(14)

$$x_m = \begin{bmatrix} 1 & 0 \end{bmatrix} \begin{bmatrix} x \\ \dot{x} \end{bmatrix} + n.$$

(15)

For this model, the external disturbances include mechanical excitation and measurement noise/error, as represented by $d$ and $n$, respectively. An extended state estimator, which incorporates the best estimate of $f$ as an additional state variable, may be considered in the form

$$\frac{d}{dt} \begin{bmatrix} \hat{x} \\ \hat{\dot{x}} \end{bmatrix} = A \begin{bmatrix} \hat{x} \\ \hat{\dot{x}} \end{bmatrix} + k_i B_d i + L(x_m - \hat{x}),$$

(16)

where $L$ is the observer gain matrix and

$$A = \begin{bmatrix} 0 & -\frac{1}{m_x} & 0 \\ -\frac{k_x}{m_x} & -\frac{c_x}{m_x} & \frac{1}{m_x} \\ 0 & 0 & 0 \end{bmatrix}, \quad B_d = \begin{bmatrix} 0 \\ \frac{1}{m_x} \\ 0 \end{bmatrix}.$$

Defining $e = \begin{bmatrix} x \\ \dot{x} \\ f \end{bmatrix} - \begin{bmatrix} \hat{x} \\ \hat{\dot{x}} \\ \hat{f} \end{bmatrix}$ then, from equations (14)-(16), the error dynamics are obtained as

$$\dot{e} = (A - LC)e + B_d d - Ln,$$

(17)
where $C = [1 \ 0 \ 0]$ and the observer gain $L$ is calculated to minimize the RMS state estimation error. If $d$ and $n$ are zero-mean Gaussian white-noise processes with covariances $Q$ and $R$, respectively, the optimal observer (Kalman filter) follows from the solution $P$ to the following matrix Riccati equation:

$$AP + PA^T - PC^TR^{-1}CP + B_dQB_d^T = 0.$$  \hspace{1cm} (18)

The realization of Equation (17) with observer gain $L = PC^TR^{-1}$ provides an optimal estimation of both the system state variables and the external interaction force. Note that, as $Q$ and $R$ are scalars, the solution for $P$ (and hence $L$) depends only on the ratio $Q/R$. Consequently, the ratio $Q/R$ may be treated as a design parameter that sets the bandwidth (cut-off frequency) for the force measurements. The value can be chosen empirically to give a suitable trade-off between low noise and fast dynamic response for the force estimation.

5.3 Results

Tests were conducted where the injection needle was moved sinusoidally to produce intermittent contact with a thin beam. As the stiffness of the beam is known, the actual interaction force could be calculated directly from the displacement. Figure 4 shows the model-based force estimate, calculated as described in sections 5.1 and 5.2, for cases with high and low stiffness settings.

Regarding the high stiffness case (see Figure 4a), the force estimate from the inverse model is contaminated by large errors. The main cause of the error is that step changes in the displacement signal due to quantization are amplified by the inverse model (Equations (12) and (13)). The cut-off frequency for the filtered derivative was set to $\omega_c = 4\pi$ rad/s in order to limit error amplification. The force estimate from the disturbance observer (Figure 4b) shows significant improvements in noise level and overall accuracy. The RMS error values for the inverse model and disturbance observer methods were 289 $\mu$N and 69 $\mu$N, respectively. For the low stiffness case (Figure 4c), the force estimate from the inverse model has much lower error levels. This can be attributed to the reduction in both $k_x$ and $c_x$.

The force estimates from the disturbance observer (see Figure 4d) show improvements in regard to less high frequency noise. However, the RMS error does not decrease significantly as the presence of low frequency disturbances causes positional drift, which is the main source of error in this case.

The results from testing with three different mechanism stiffness settings are summarized in Table 3. For the inverse model method, the effect from the stiffness reduction gives clear improvements in force-sensing accuracy, as the dominant source of error is the quantization of the displacement signal due to quantization error from the position sensor. Since the success of this approach relied on an accurate system model, a practical scheme was introduced to identify coefficients for a single-degree-of-freedom mechanism model. The findings reported here indicate there was good potential for using the technique in automated

| Table 3. Summary of force estimation results. |
|-----------------------------------------------|
| Case | $k_x$ (N/m) | RMS force estimate error: $\sigma(f - \bar{f})$ (\(\mu\)N) | |
|------|-------------|-------------------------------------------------|---|
| A    | 656.7       | 289                                           | 69 |
| B    | 329.4       | 196                                           | 82 |
| C    | 104.4       | 133                                           | 63 |

6. Conclusions

This study investigated a sensorless force estimation method for a flexure-based micro-injection mechanism. A model-based disturbance estimation scheme with optimal state observer was introduced to obtain real-time estimates of interaction forces. The main limitations of the approach were related to model inaccuracy, noise, and disturbance effects. In particular, this included noise and quantization error from the position sensor. Since the success of this approach relied on an accurate system model, a practical scheme was introduced to identify coefficients for a single-degree-of-freedom mechanism model. The findings reported here indicate there was good potential for using the technique in automated
cell injection. Further work is needed to examine the utilization of the force-estimates within real-time control of the micropipette motion during cell micro-injection procedures.

**Figure 4.** Comparisons of the results of the contact force estimation obtained from the inverse model and disturbance observer

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