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Department of Electrical Engineering and Information Technology
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Control Channel Routing for Matrix-Based Continuous-Flow Microfluidic Biochips

Bachelor Thesis

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Abstract

Microfluidic flow-based biochips are taking the place of conventional biological laboratories by using their microfluidic very large scale integration technology. Manual design procedures are still the mainstream in the present, but they are hard to be applied to complex experimental design. At present, researches of matrix-based biochip automation are relatively less so that the design automation for control layer in the matrix-based biochip has not realized. In this work, we present a computer-aided design for control layer in the matrix-based continuous-flow mircofluidic biochip to improve the routability of valves and reduce the count of ports, which cannot be supported by previous work. We first introduce the control channel routing problem for matrix-based biochip and then propose an integer-linear-programming (ILP) model for solving this problem. In this model, we use the characteristics of working pattern to implement that multiple valves can be connected with control channels to one port. Therefore, the goals of our design can be achieved.

Acknowledgements

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1. Introduction

Continuous-flow microfluidic biochips have made significant progress in recent decades. This composite microsystem, also known as Lab on a Chip, is a integrating device of biochemical laboratory equipments such as micropumps, microvalves, chamber, etc. It can contain one million components per square centimeter (Araci & Quake 2012) by using soft lithography and monolithic integration fabrication technology. Compared with traditional laboratory procedure, mircofluidic biochip can provide much more advantages including lower fabrication cost, lower reagent volume, lower sample and energy consumption, and time saving. For example, application of microfluidic biochip for blood typing test only require a smaller reagent volume (about 3 μl) than the conventional methods (more than 20 μl) (Kim et al. 2006). In addition, using microluidic channel of biochip for blood typing test also can increase surface to volume ratio so that it could shorten reaction time of agglutinins in serum, thereby resulting in less time (Kim et al. 2006).

Matrix-based continuous-flow microfluidic biochip is based on valve-centered control system, which consist of pressure sources, control channels lying in the control layer and flow channels lying in the flow layer (Tseng et al. 2015) and is used to manipulate the fluids (i.e., samples/reagents) flow direction by switching valves. Valve is formed by overlooping position of flow and control channel from their respective layers. Control channel is connected to the port and external pressure source. If control channel is pressurized then the valve will be closed, otherwise, valve will be opened. Thus, diverse operations such as cell culturing, reaction of reagents or detection can be performed in a single chamber (Baudoin et al. 2007), which is a segment of flow channels surrounded by four valves in a matrix-based microfluidic biochip.

But there is a fact that is often overlooked in the previous work: If a larger experiment requires extra chambers to perform more operations in same matrix-based biochip, then the amount of valves also should be increased. For example, if the experiment need to add n chamber to each boundary of the layer, then the total number of chambers grows as $\mathcal{O}(n^2)$ and the total number of valves also grows as $\mathcal{O}(n^2)$, but the amount of ports grows as $\mathcal{O}(n)$ in the matrix-based biochip. If n has been large enough, then a port can not assign single valve in a matrix-based biochip so that the microsystem cannot operate properly. Thus, the requirement in control layer design is by connecting one port to multiple valves to reduce the amount of ports.

Lately, several studies have pay attention to the issue and put forward their solutions. In (Yao et al. 2015): Compatible valves in conventional microfluidic biochip are connected with control channels of equal length to the inlets. If this precondition is to satisfy, then compatible valves can also be assigned to the same inlet. Thus the compatible valves can be actuated simultaneously and the amount of inlets can be reduced. In (Hu et al. 2016): The ports can be placed anywhere in the chip and valves can be set depend on the positions of ports so that the routability of valves can be increased. Compatible valves can be connected to the same port so that the amount of ports can be minimized. However, since valves in matrix-based biochip are arranged regularly with different *working pattern* (activation sequence), above methods cannot be applied to our work. In (Yan & Wong 2009): The escape routing model is used to guarantee the routability. But the valves cannot share their pressure with each other, so that the number of ports can not be reduced. In conclusion, the goals of this work are to guarantee the routability of valves and minimize the amount of ports in matrix-based microfluidic biochip.

To achieve goals above, we first introduce the control channel routing problem, then we build integer-linear-programming (ILP) model for solving this problem. But this model is to complex for the current optimization solver. Therefore, I will continue to do this project by programming and application of heuristic methods such as dijkstra's shortest path algorithm until control channel routing network can be formed automatically.

The rest of this paper is organized as follows: Section 2 introduces some background information. Section 3 presents our integer-linear-programming (ILP) model. Finally, conclusion and future work are drawn in Section 4.

2. Device Architecture and Operation

In this section, we first introduce developing trends and main existing problems of matrix-based continuous-flow microfluidic biochips. Next, we highlight the specific characteristics of matrix-based microfluidic biochips. Then we present the formal statement for the routing problem of control layer.

2.1. Background

Matrix-based continuous-flow microfluidic biochips have evolved rapidly in the last decades. We show a general control channel network of a matrix-based microfluidic biochip in Figure 2.1(b) (Fidalgo & Maerkl 2011). By increasing the integration levels and design complexity, sophisticated bioassays can be automatically and independently performed in one matrix-based continuous-flow microfluidic biochip. This technology contributes greatly to the high-throughput deoxyribonucleicacid (DNA) sequencing (Xu & Chakrabarty 2008), biochemical analyses and point-of-care diagnosis of diseases (Hu et al. 2016). Using current production technology has also realized the mass fabrication of biochips. However, manual design procedures for matrix-based continuous-flow microfluidic biochip are still the mainstream in the present which lead to high design cost and suppress automated processes of matrix-based biochips (Hu et al. 2016). Hence, we will enable automation of design for control layer in matrix-based biochip.

2.2. Architecture

The structural discrepancy between conventional continuous-flow microfluidic biochip and matrix-based continuous-flow microfluidic biochip embodies in the different positions of valves and ports. In the conventional microfluidic biochip, ports can be set anywhere on the layer. Therefore, valves can be set based on the position of their ports as shown in Figure 2.1(a) (Tseng

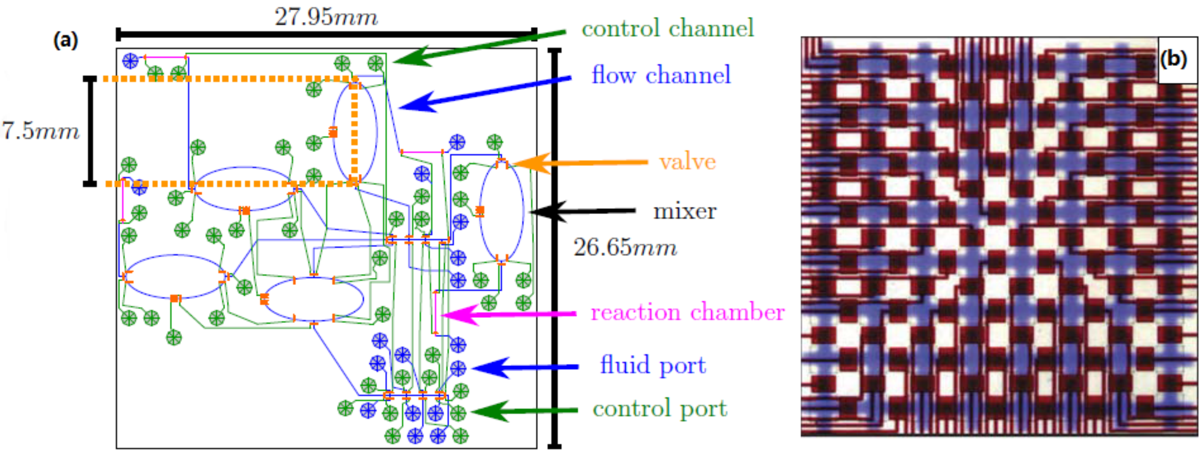

Figure 2.1.: (a) Model of conventional continuous-flow microfluidic biochip. (b) Model of matrix-based continuous-flow microfluidic biochip.

et al. 2016). But in the matrix-based microfluidic biochip, ports can only be placed at the boundaries of the layer and valves must be arranged regularly as shown in Figure 2.1(b) (Fidalgo & Maerkl 2011). Next, the main components of matrix-based microfluidic biochip will be introduced.

2.2.1. Port

All ports on a microfludic biochip have identical physical properties and can be devided in to inlets and outlets. In the matrix-based biochip, ports can only be set on boundaries of the control layer and connected with control channels to external pressure sources.

2.2.2. Valve

Valve is formed by overlooping position of control and flow channels from their respective layers. Figure 2.2(a) (Hu et al. 2016) shows a general valve structure of a two-layer flow-based biochip . By switching valves we can manipulate the direction of fluid flows. When a valve is open, fluids can flow unimpeded through the valve along the flow channel. In order to close the valves, we need to pump oil or air from their pressure sources into their control channels, which can be inflated so that fluids can not pass through the valve underneath. Thus, the direction of flows can be controlled. In this work, we apply *working pattern* to illustrate the activation of valves during program runtime (Tseng et al. 2015).

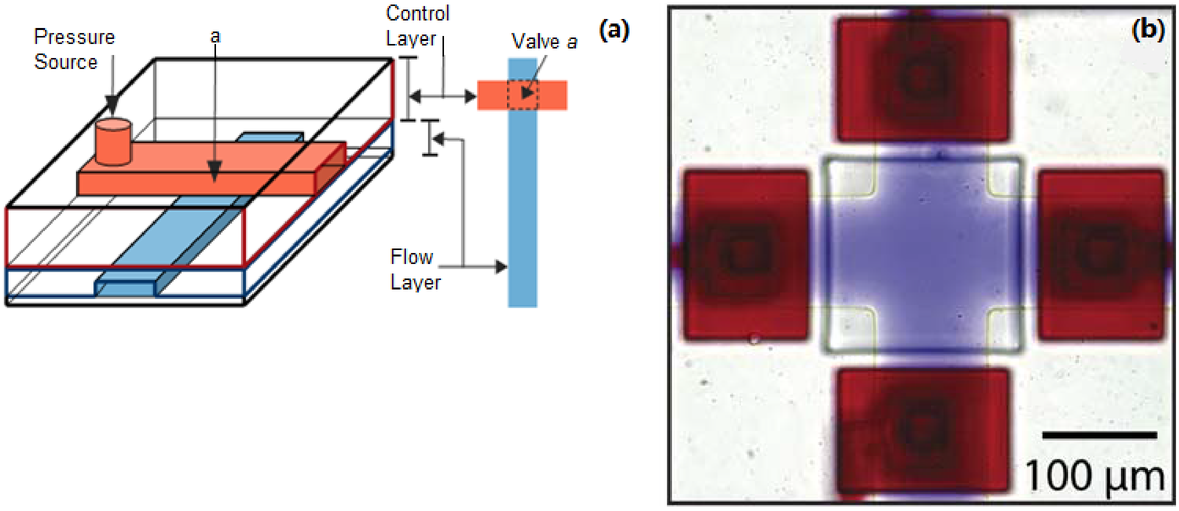

Figure 2.2.: (a) Model of a valve. (b) Model of a chamber.

In (Yao et al. 2015), the definitions of compatible valve and working pattern are given, but they have not consider pump valve situation. Thus, based on the work of (Yao et al. 2015), we add pump valve situation in working pattern and define the compatible valve in a matrix-based microfluidic biochip as follows:

Definition 1 *(Working pattern). $W(v) = (x_1, x_2, \ldots, x_n)$ for valve v is called a working pattern, where x_i denotes the valve status ("0", "1", "P", "X") at time step i, and n is the total number of time steps.*

As shown in Figure 2.3, "0" means opened valve, i.e., low pressure in the control channel. "1"indicates that the valve is closed, i.e., high pressure in the control channel. "P" at a valve means that the valve is a pump valve, which provide pressure for fluid movement. "X" means that the valve can be set to any status. In "X" situation, the valve is not a part of device control / wall valve and there is no fluid flowing by this valve, therefore the valve can be closed or opened. Since it will not have any effect on current device operation, this valve can be also a pump valve.

Definition 2 *(Compatible valve status). Valve status x_i and x_j are compatible, denoted as $x_i \cong x_j$,if and only if any of the following conditions are satisfied: (1) x_i=x_j, (2) x_i=X, (3) x_j=X.*

Definition 3 *(Compatible working pattern). $W(v_k) = (x_{k1}, x_{k2}, \ldots, x_{kn})$ and $W(v_l) = (x_{l1}, x_{l2}, \ldots, x_{ln})$*

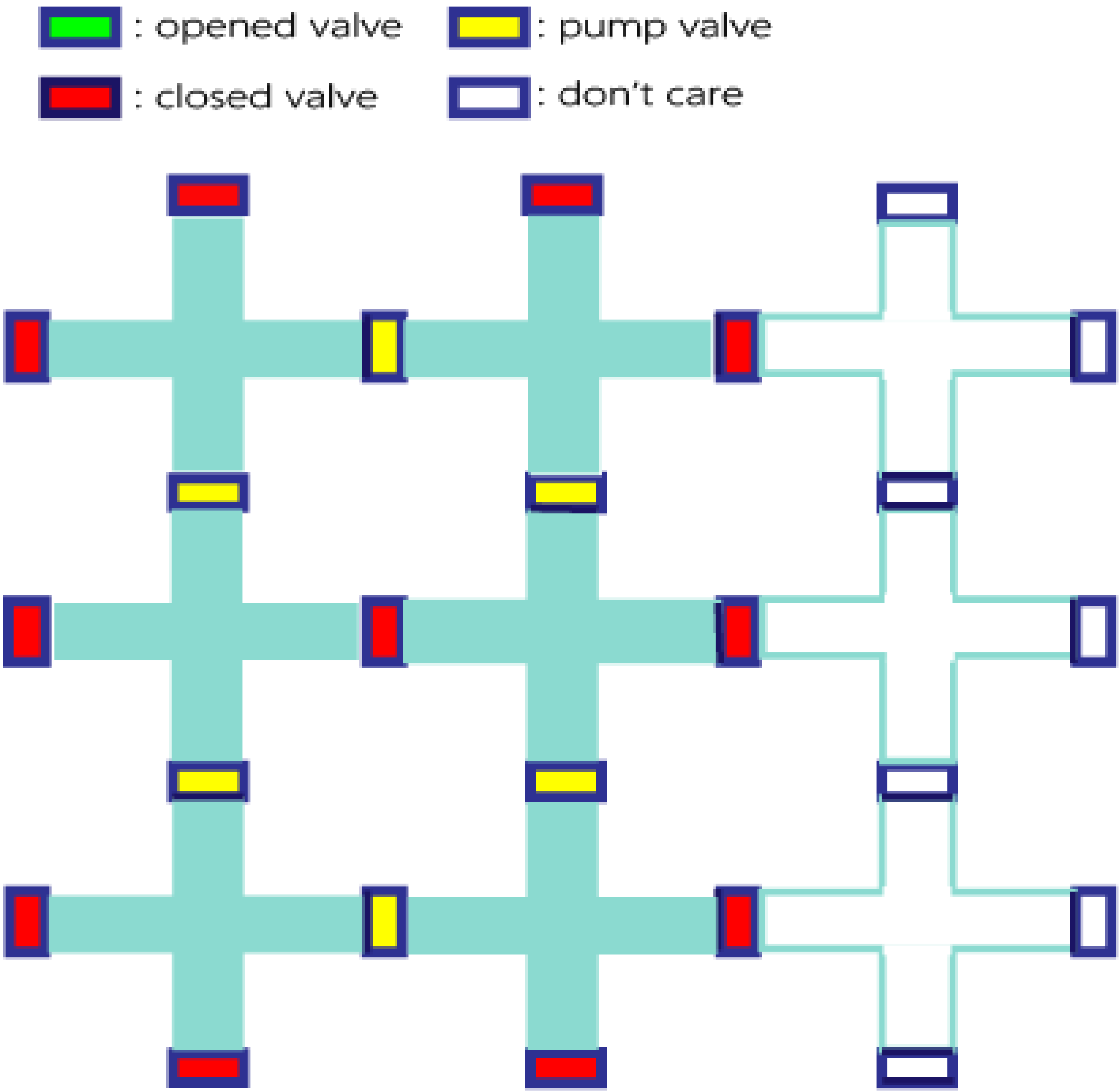

Figure 2.3.: A 3 × 3 dynamic mixer.

are compatible, denoted as $W(v_k) \cong W(v_l)$ *if and only if* $\forall\ 1 \leq i \leq n\ ,\ x_{ki} \cong x_{li}$.

Definition 4 *(Compatible valve). Valve* v_k *and valve* v_l *are compatible, denoted as* $v_k \cong v_l$ *if and only if* $Wv_k \cong Wv_l$.

Thus, the compatible valves can be assigned to a same port in order to minimize the count of ports.

2.2.3. Chamber

Chamber is a segment of flow channels surrounded by four valves in a matrix-based microfluidic biochip as shown in Figure 2.2(b) (Fidalgo & Maerkl 2011). Different types of operations such as mixing (White et al. 2011), separation (Baudoin et al. 2007), detection (Baudoin et al. 2007), neutralization (Marcy et al. 2007), and cell culturing (Gomez-Sjoeberg et al. 2007) can be performed in chambers.

2.3. Problem Formulation

Therefore, the control channel routing problem that we are dealing with can be formulated as follows:

Input :

(1) Location of valve. (2) Working pattern of valve.

Output :

The implementable control channel routing paths.

Objective :

(1) Implement routability of valves. (2) Reduce number of ports.

3. Control Channel Routing Model

As shown in Figure 3.1, a routing network is composed of nodes, valves and control channels. In our design, the compatible valves in matrix-based biochip can be connected to each other with control channels through the node. The main goal of the model concept is to connect compatible valves as much as possible under the routability of valve. Thus, this section presents the integer-linear-programming (ILP) of model for node and valve to improve the routability and reduce the number of ports in matrix-based biochip.

3.1. Node Model

The direction of pressure in control channel can be changed or maintained while passing through the node, where is the point in the control layer network at which control channels may intersect.

3.1.1. Location and Direction

In this work, a control channel routing model is presented based on the coordinate system as shown in Figure 3.2. (i, j) represents the center coordinate of valve, chamber or node unit. We define $\forall(i, j) = \{2 \times s; s \in \mathbb{N}\} \times \{2 \times d; d \in \mathbb{N}\}$ as the locations of node units in the model. Node unit is divided into four node groups. We number the groups by k, where $k \in \{0, 1, 2, 3\}$. Thus, we denote the $k-th$ group in node unit (i, j) as (i, j, k). A node group can consist of $w \times w$ nodes, where w is the amount of tracks with $w \in \mathbb{N}$. We number the nodes in group by l, where $l \in \mathbb{N}, 1 \leq l \leq w^2$, so that the $l-th$ node in $k-th$ group of node unit (i, j) is denoted by (i, j, k, l).

The node in our model can be connected with control channels in four directions as shown in Figure 3.3(a). We number the directions by m with $m \in \{0, 1, 2, 3\}$. Therefore, the $m-th$ direction of node (i, j, k, l) can be denoted by (i, j, k, l, m). We introduce a binary variable

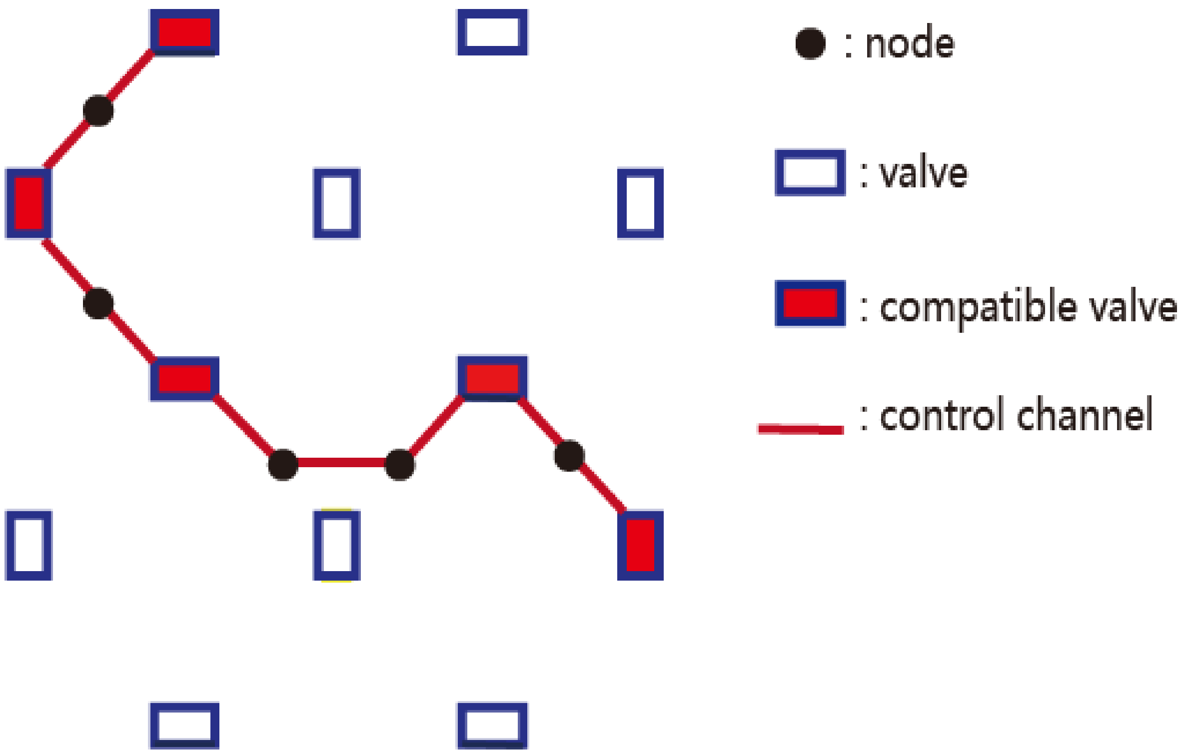

Figure 3.1.: An example of a routing model in 2 × 2 mixer device with 1 × 1 tracks.

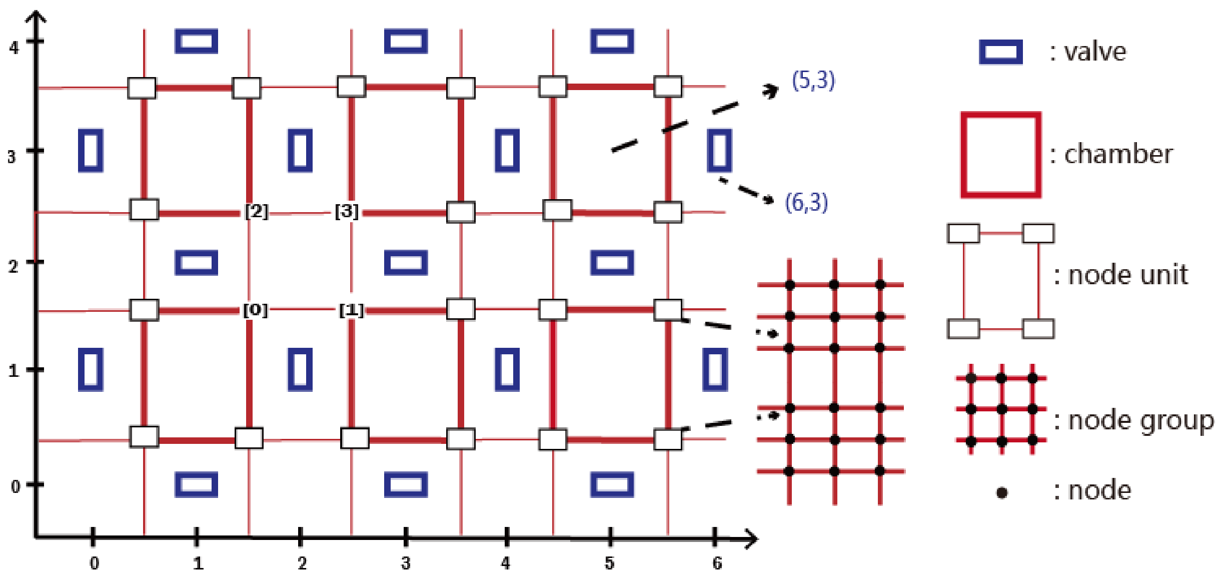

Figure 3.2.: A part of a control layer routing model with 3 × 3 tracks.

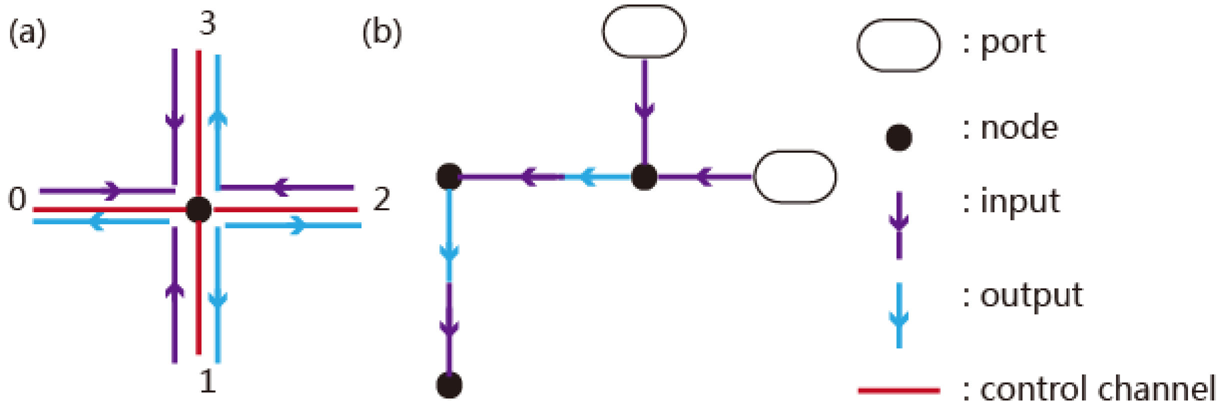

Figure 3.3.: (a)Control channel directions, pressure receiving and delivery of node model. (b)Example for multiple inputs of node.

$b_{i,j,k,l,m}$ to indicate the existence of control channel in $m-th$ direction of node (i,j,k,l). $b_{i,j,k,l,m}$ can be interpreted as:

$$b_{i,j,k,l,m} = \begin{cases} 0 & \text{if control channel do not exist} \\ 1 & \text{if control channel exist} \end{cases} \tag{3.1}$$

Correspondingly, the amount of control channels for node (i,j,k,l) can be calculated. In our concept, ports are not included in the category of node. Therefore, if the node (i,j,k,l) exists, it must be connected at least with two control channels in order to transform pressure. Since a node can be connected with control channels in four directions, the amount of control channels for node is limited to four. Thus, the amount of control channels for node (i,j,k,l) can be set to 2, 3 or 4. If node (i,j,k,l) do not exists, which means there is no control channel passing through the node, then the amount of control channels for this node will be set to 0. Here, we introduce $H_{i,j,k,l}$ to indicate the amount of control channels for node (i,j,k,l) and formulate $H_{i,j,k,l}$ as:

$$\sum_{m=0}^{3} b_{i,j,k,l,m} = H_{i,j,k,l}, \tag{3.2}$$

$$H_{i,j,k,l} = 1 - q_0 + \sum_{r=1}^{3} r \times q_r, \tag{3.3}$$

$$\sum_{r=0}^{3} q_r = 1. \tag{3.4}$$

where q_r is an auxiliary binary variable with $r \in \{0,1,2,3\}$.

3.1.2. Pressure Receiving and Delivery

As mentioned previously, node can receive or transmit pressure to change or maintain pressure direction of control channel. We define pressure receiving of control channel as *input channel* and pressure delivery of control channel as *output channel*.

In our concept, if node exists, then it can have at most one input channel. We explain this design by example in Figure 3.3(b): The node on the top right corner has two input channels, which means it can be connected with control channels to two ports. However, in this situation, pressure from one port is already sufficient, which means that the other port is redundant. In our model, we confine the number of input channels for one node is equal to or fewer than 1 by introducing the following constraints:

$$\sum_{m=0}^{3} \alpha_{i,j,k,l,m} \leq 1. \tag{3.5}$$

in which $\alpha_{i,j,k,l,m}$ is binary variable to represent existence of input channel in $m-th$ direction for node (i,j,k,l). If $\alpha_{i,j,k,l,m}$ is chosen to be 1, then node (i,j,k,l) has a input channel in $m-th$ direction. If $\alpha_{i,j,k,l,m}$ is chosen to be 0, which means there is no input channel in $m-th$ direction for node (i,j,k,l).

If there is no control channel passing through the node (i,j,k,l), which means the amount of control channels for this node is set to 0 ($i.e.$, $H_{i,j,k,l} = 0$), then the total number of input is also set to 0. This can be formulated as:

$$M \times \sum_{m=0}^{3} \alpha_{i,j,k,l,m} \geq H_{i,j,k,l}, \tag{3.6}$$

$$\sum_{m=0}^{3} \alpha_{i,j,k,l,m} \leq H_{i,j,k,l}. \tag{3.7}$$

in which M is a very large constant.

In our concept, if node exists, then it can have multiple output channels but only one input channel. Since the node has already one input channel, the number of output channels can be set to 1, 2 or 3. If there is no control channel passing through the node (i,j,k,l), which means the amount of control channels for this node is set to 0, then the total number of input and output is also set to 0. If node (i,j,k,l) is connected with one input channel, then the rest

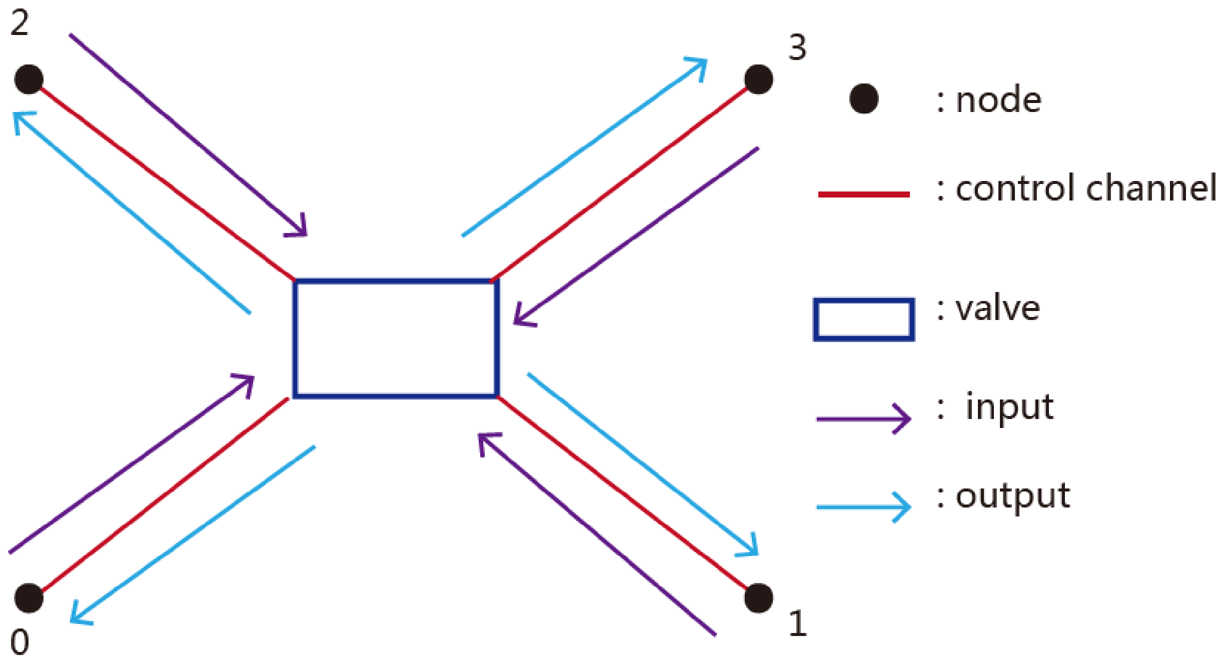

Figure 3.4.: Pressure directions of valve.

of control channels should be the output channels. Thus, sum of input channel and output channels is equal to the amount of control channels. If the control channel in $m-th$ direction exists, then input and output can not be activated simultaneously in the same control channel. Thus, the constraint can be formulated as:

$$\alpha_{i,j,k,l,m} + \gamma_{i,j,k,l,m} = b_{i,j,k,l,m}. \tag{3.8}$$

in which $\gamma_{i,j,k,l,m}$ is binary variable to represent existence of output channel in $m-th$ direction for node (i, j, k, l). If $\gamma_{i,j,k,l,m}$ is chosen to be 1, then node (i, j, k, l) has a output channel in $m-th$ direction. If $\gamma_{i,j,k,l,m}$ is chosen to be 0, which means there is no output channel in $m-th$ direction for node (i, j, k, l).

3.2. Valve Model

3.2.1. Location and Direction

As shown in Figure 3.2, the center coordinates $(i, j) = \{2 \times s; s \in \mathbb{N}\} \times \{2 \times d + 1; d \in \mathbb{N}\} \cup \{2 \times s + 1; s \in \mathbb{N}\} \times \{2 \times d; d \in \mathbb{N}\}$ represent the locations of valves.

In our concept, valve can receive or transmit pressure in four directions as shown in Figure 3.4, which means it can be connected with at most four control channels to nodes. We number the directions of pressure for valve (i, j) by n with $n \in \{0, 1, 2, 3\}$. Therefore, the $n-th$ direction of valve (i, j) can be denoted by (i, j, n). We introduce binary variable $b_{i,j,n}$ to indicate existence of control channel in $n-th$ direction of valve (i, j). Their relation can be formulated as:

$$b_{i,j,n} = \begin{cases} 0 & \text{if control channel do not exist} \\ 1 & \text{if control channel exist} \end{cases} \tag{3.9}$$

In order to guarantee the routability, each valve must be connected with at least one control channel through nodes to a port. Since a valve can be connected with control channels in four directions, the amount of control channels for valve is limited to four. Thus, the amount of control channels for valve (i, j, k, l) can be set to 1, 2, 3 or 4. It can be introduced as:

$$\sum_{n=0}^{3} b_{i,j,n} \geq 1. \tag{3.10}$$

3.2.2. Pressure Receiving and Delivery

As mentioned in node model, pressure receiving of control channel is interpreted as *input channel* and pressure delivery is denoted as *output channel*. Each valve must have at least one input channel in order to be actuated, so that the routability can be guaranteed. Analogous to node model, valve can receive pressure from one direction to reduce the number of ports. Thus, the amount of control channels for valve (i, j) can be represented as:

$$\sum_{n=0}^{3} \alpha_{i,j,n} = 1. \tag{3.11}$$

in which $\alpha_{i,j,n}$ is binary variable to represent existence of input channel in $n-th$ direction for valve (i, j). If $\alpha_{i,j,n}$ is chosen to be 1, then valve (i, j) has a input channel in $n-th$ direction. If $\alpha_{i,j,n}$ is chosen to be 0, which means there is no input channel in $n-th$ direction for valve (i, j).

Since the amount of control channels is limited to four and valve has already one input channel, the number of output channels can be set to 0, 1, 2 or 3 and the sum of input channel and output channels is equal to the amount of control channels. Furthermore, pressure can not be simultaneously received and transmitted in the same control channel. This can be represented as:

$$\alpha_{i,j,n} + \gamma_{i,j,n} = b_{i,j,n}. \tag{3.12}$$

in which $\gamma_{i,j,n}$ is binary variable to represent existence of output channel in $n-th$ direction for valve (i,j). If $\gamma_{i,j,n}$ is chosen to be 1, then valve (i,j) has a output channel in $n-th$ direction. If $\gamma_{i,j,n}$ is chosen to be 0, which means there is no output channel in $n-th$ direction for valve (i,j).

3.2.3. Routing Network of Valve

The model from *Section* 3.2.2 can guarantee routability of each valve. Hence, in this section we will improve our current model to reduce the count of ports in the matrix-based biochip.

In order to reduce count of ports, compatible valves can be connected with each other to one port. According to Definition 1 ($Page12$), each valve with coordinate (i,j) has its original working pattern $W(v_{i,j}) = (x_{i,j,1}, x_{i,j,2}, \ldots, x_{i,j,z})$, where z is the size of time steps. Valve can be assigned by the working pattern, which is compatible with its original working pattern. If valve (i,j) and valve (λ,μ) are compatible but $x_{i,j,z} = X$ and $x_{\lambda,\mu,z} \neq X$, then the $z-th$ status of valve (i,j) must be equal to $z-th$ status of valve (λ,μ), which means $x_{i,j,z} = x_{\lambda,\mu,z} \neq X$. If valve (i,j) is connected to valve (λ,μ), then the working pattern of valve (i,j) will be changed and more precise (i.e less "X"). This can be illustrated by the next example: The working patterns of valve $(6,3)$ and valve $(5,2)$ are given as:

$$W(v_{6,3}) = (1,0,1,P,X,P,X,0), \tag{3.13}$$

$$W(v_{5,2}) = (X,0,1,P,1,X,P,0). \tag{3.14}$$

According to Definition from $Page12$, $W(v_{6,3})$ and $W(v_{5,2})$ are compatible working patterns, so that valve $(6,3)$ and $(5,2)$ are also campatible. If valve $(6,3)$ and valve $(5,2)$ are connected to the same port in network, then working patterns of both valves must be changed to $(1,0,1,P,1,P,P,0)$. If we do not change working pattern of valve $(6,3)$ and use $W(v_{6,3})$ to assign valve $(6,3)$ and $(5,2)$, then other valves with working patterns $(1,0,1,P,P,P,X,0)$, $(1,0,1,P,0,P,X,0)$, etc., which are not compatible with valve $(5,2)$, can also be connected to valve $(6,3)$ and $(5,2)$, which contradicts with the premises of our concept. Therefore, the working pattern of valves must be changed precise and new working pattern such as $(1, 0, 1, P, 1, P, P, 0)$ can be given.

Next, we will select and number working patterns, which can assign one or multiple valves.

Step 1 We denote the total number of valves by Y_1 and number all valves by y_1, where $y_1, Y_1 \in \mathbb{N}, 1 \leq y_1 \leq Y_1$. We give also same numbers to their original working patterns and add them to list of candidate working patterns, which is empty before.

Step 2 We compare working patterns with number y_1 from 1 to Y_1 one to one. If the working patterns compare as compatible but not equal, then new working patterns will be generated as shown in example and added to the list of candidate working patterns. We select from candidate list the working patterns, which can assign two compatible valves, and number them by y_2 with $Y_1 < y_2 \leq Y_2$, where Y_2 is the total number of working patterns, which can assign one or two valves.

Step 3 We compare working patterns with number y_2 from $Y_1 + 1$ to Y_2 one to one. If the working patterns compare as compatible but not equal, then new working patterns will be generated and added to the list of candidate working patterns. We choose from candidate list the working patterns, which can assign three compatible valves, and number them by y_3 with $Y_2 < y_3 \leq Y_3$, where Y_3 is the total number of working patterns, which can assign one, two or three valves.

Step ..

Step d We compare working patterns with number y_{d-1} from $Y_{d-2} + 1$ to Y_{d-1} one to one. If the working patterns compare as compatible but not equal, then new working patterns will be generated and added to the list of candidate working patterns. We choose from candidate list the working patterns, which can assign d compatible valves and number them by y_d with $Y_{d-1} < y_d \leq Y_d$, where Y_d is the total number of working patterns, which can assign $1, 2, \ldots,$ or d valves.

The total number of working patterns is denoted by Y_d.

Thus, a valve can be assigned by working patterns in candidate list, which are compatible with its original working pattern. However, in the routing network, a valve can be assignd only by one working pattern. If the valve (i, j) is already connected, then its working pattern should be identical with connected valves or port and can not be changed anymore. We introduce set $C_{i,j}$ to represent all numbers of working patterns, which can assign valve (i, j) to another valves or port, and propose $c_{i,j,s}$ with $1 \leq s \leq |C_{i,j}|$ as element to represent the number of each working pattern in the set $C_{i,j}$. We propose integer $I_{i,j}$ to represent the current number of working pattern, which can assign valve (i, j), it can be formulated as:

$$I_{i,j} = \sum_{s=1}^{|C_{i,j}|} c_{i,j,s} \times a_s, \tag{3.15}$$

$$\sum_{s=1}^{|C_{i,j}|} a_s = 1. \tag{3.16}$$

where a_s is an auxiliary binary variable. The $No.c_{i,j,s}$ working pattern is selected if a_s is set to 1.

A valve must be connected with control channels through node to port or another valves with same working pattern. Thus, we also give the working patterns to control channels and nodes. The number of working patterns for control channels should be identical with the number of working pattern for valve, which the control channels can be connected with. Hence, we introduce $I_{i,j,n}$ to represent the number of working pattern for control channel (i.e. input channel or output channel) in $n-th$ direction of valve (i, j). In this phase, if the input channel in $n-th$ direction of valve (i, j) exists, which means $\alpha_{i,j,n}$ is set to 1, then the number of working pattern for input channel and valve should be identical. This relation can be formulated as:

$$I_{i,j,n} \leq I_{i,j} + (1 - \alpha_{i,j,n}) \times M, \tag{3.17}$$

$$I_{i,j,n} \geq I_{i,j} - (1 - \alpha_{i,j,n}) \times M. \tag{3.18}$$

where M is a very large constant. If the output channel in $n-th$ direction of valve (i, j) exists, which means $\gamma_{i,j,n}$ is set to 1, then the number of working pattern for output channel and valve should be identical. This relation can be formulated as:

$$I_{i,j,n} \leq I_{i,j} + (1 - \gamma_{i,j,n}) \times M, \tag{3.19}$$

$$I_{i,j,n} \geq I_{i,j} - (1 - \gamma_{i,j,n}) \times M. \tag{3.20}$$

where M is a very large constant.

The control channel in $n - th$ direction of valve can be the same channel as in $m - th$

direction of node. The number of working patterns for control channel in $m-th$ direction of node should be identical with the number of working pattern for node so that valve can be connected with control channels to nodes and the routing network can be formed. Analogous to control channel, we give working pattern to node and propose $I_{i,j,k,l}$ to represent the number of working pattern for node (i,j,k,l) and $I_{i,j,k,l,m}$ to indicate the number of working pattern for control channel in $m-th$ direction of node (i,j,k,l). In this phase, if node (i,j,k,l) and input channel in $m-th$ direction exist, which means $I_{i,j,k,l}$ is set to positive and $\alpha_{i,j,k,l,m}$ is set to 1, then the number of working pattern for node and input channel should be identical. This relation can be formulated as:

$$I_{i,j,k,l,m} \leq I_{i,j,k,l} + (1-\alpha_{i,j,k,l,m}) \times M, \tag{3.21}$$

$$I_{i,j,k,l,m} \geq I_{i,j,k,l} - (1-\alpha_{i,j,k,l,m}) \times M. \tag{3.22}$$

where M is a very large constant. If the output channel in $m-th$ direction of node (i,j,k,l) exists, which means $\gamma_{i,j,k,l,m}$ is set to 1, then the number of working pattern for output channel and node should be identical. This relation can be formulated as:

$$I_{i,j,k,l,m} \leq I_{i,j,k,l} + (1-\gamma_{i,j,k,l,m}) \times M, \tag{3.23}$$

$$I_{i,j,k,l,m} \geq I_{i,j,k,l} - (1-\gamma_{i,j,k,l,m}) \times M. \tag{3.24}$$

where M is a very large constant. Therefore the valve (i,j) can be connected through node along control channels with same working pattern to port or compatible valves.

However, the routing network may form a deadloop if all conditions are met as shown in Figure 3.5(a). In this situation, the input channel is connected with output channel from same valve so that the valve cannot receive or transmit any pressure and cannot be connected to port or other valves. Since input channel and output channel with same working pattern can be connected with same valve, we need to change the number of working pattern for output channel, so that the input channel and output channel from same valve can not be connected with each other. Thus, we add a periode for each number of working pattern, so that each working pattern has a number interval. The valve can be connected to the other valves, if their working pattern numbers in same interval. We introduce integer T as the total number of valves in matrix-based biochip to represent periode for each number and integer t with $0 \leq t \leq T-1$. Hence, the interval $[1 + T \times c_{i,j,s}, 1 + T \times c_{i,j,s} + T - 1]$ represents working pattern $No.\ c_{i,j,s}$ and each valve can be assigned only by one working pattern, which means

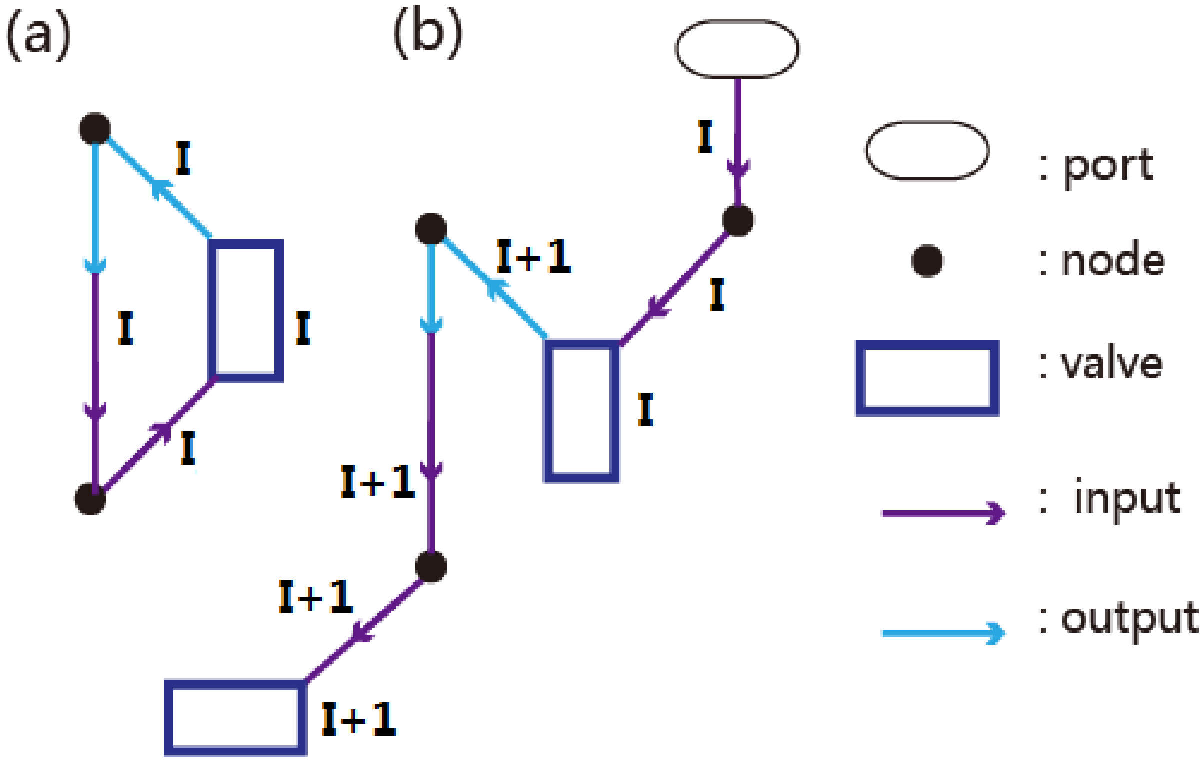

Figure 3.5.: (a) Deadloop problem. (b)Solution for deadloop.

$I_{i,j}$ can only be set to the number in one intervall. It can be formulated as:

$$I_{i,j} = \sum_{s=1}^{|C_{i,j}|} (1 + c_{i,j,s} \times T) \times a_s + t, \tag{3.25}$$

$$\sum_{s=1}^{|C_{i,j}|} a_s = 1. \tag{3.26}$$

where a_s is an auxiliary binary variable. The working pattern $No.c_{i,j,s}$ is selected if a_s is set to 1.

In our current concept, the working patterns of input channels should be identical with the working pattern of their valve. The formulation of working pattern for input channel is the same as (3.17), (3.18). In order to find the other compatible valves with working pattern number in same interval, the number of working pattern for output channel from each valve can be increased by 1 as shown in Figure 3.5(b). This relation can be formulated as:

$$I_{i,j,n} \leq I_{i,j} + (1 - \gamma_{i,j,n}) \times M + 1, \tag{3.27}$$

$$I_{i,j,n} \geq I_{i,j} - (1 - \gamma_{i,j,n}) \times M + 1. \tag{3.28}$$

But if $I_{i,j} = 1 + T \times c_{i,j,s} + T - 1$ (i.e. $t = T - 1$), then the number of working pattern for output channel of valve (i, j) can not be increased anymore or valve will be connected to other valves with different working patterns. Hence, if $I_{i,j} = 1 + T \times c_{i,j,s} + T - 1$, then the output channel of valve (i, j) do not exist, which means $\gamma_{i,j,n} = 0$ with $t = T - 1$. This can be formulated as:

$$\gamma_{i,j,n} \leq (T - 1 - t) \times M. \tag{3.29}$$

The relations for number of working patterns between node and control channel is maintained as (3.21), (3.22), (3.23), (3.24). Thus, the deadloop situation can be solved by the new model as shown in Figure 3.5(b).

4. Conclusion and Future Work

In this work, to obtain a more general understanding on control channel routing problem for matrix-based continuous-flow microfluidic biochip, we first described the background knowledge of matrix-based biochip, then the important microfluidic components and working operations have been introduced. Next, We built an integer-linear-programming (ILP) model to solve routing problem of control layer in matrix-based microfluidic biochip. In the model, sub-model as node and valve are constructed.

For the future work, since the integer-linear-programming (ILP) model is to large for the current optimization solver, we will propose heuristic methods such as Dijkstra's shortest path algorithm to solve control channel routing problem for matrix-based biochip. We will apply C++ language for routing programming. Once we get the experimental result, the routing network will be illustrated. This future work aims at automatically generating a control channel routing network of matrix-based biochip by using our program.

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