# One Lab, Two Firms, Many Possibilities

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"After chemotherapy failed to cure Emily Whiteheads severe form of leukaemia, Oxford BioMedica's new treatment has given her five cancer-free years. (...) In two weeks, America's Food and Drug Administration will put the treatment devised by Oxford BioMedica, in league with Swiss pharmaceutical giant Novartis, before a panel of independent experts. If they like the findings from the human trials, it could pave the way for a full approval in October. A European Medicines Agency filing could follow later this year."

(Sabah Meddings, July 2 2017, The Sunday Times, UK)

# Research questions

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1) does more R&D outsourcing imply less internal activity?

2) how are R&D benefits distributed among contracting parties?

3) do firms pay more for equity than for contracted-out R&D?

# Results Preview

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- internal/external operations neither substitutes nor complements;
- an aggregate measure of technological externalities drives the distribution of industry profits;
- likely abandonment of projects with economic and medical value as a likely consequence of outsourcing;
- founders of a research biotech (more than of a clinical services unit) reappropriate industry profits by selling out the equity.

# Stylized facts

1) 16.6% annual growth rate of R&D outsourcing worldwide, expenses from US$ 14 bn in 2003 to 47 bn in 2011 (Morton and Kyle, 2012).

2) from mid 70s onward "[v]irtually every new entrant ... formed at least one, and usually several, contractual relationships with established pharmaceutical (and sometimes chemical) companies" (Pisano, 2006).

3) "... a number of cases of the opposite philosophy, adding in-house research where it previously didn't exist, is also occasionally in evidence" (Rydzewski, 2008).

# Stylized facts

4) contract usually designed by the demand side (pharma firms can "go for it alone"; financial constraints faced by specialized units; high entry rate on supply side; see Arora et al., 2004; Golec and Vernon, 2009).

5) complex clauses connect payments received by external unit from a client firm and the R&D supplied to a competitor ("right of first refusal", "right to match offer", see Folta, 1998; Hagedoorn and Hesen, 2007).

6) "Uncertainty related to the success/failure of R&D activities is the major concern for R&D managers in the biopharmaceutical industry" (Pennings and Sereno, 2011).

# Related literature (theory)

Aghion and Tirole (1994): exclusive division of R (upstream) and D (downstream), relative efficiency of efforts drives separation/integration, no downstream competition.

Anton and Yao (1994): no endogenous R&D effort, two client firms with sequential bargaining, secret reselling, focus on profit distribution.

Bhattacharya and Guriev (2006, 2013): endogenous D effort chosen by two client firms, secret reselling, information leaks, focus on contractual form ("open form & exclusivity" vs. "closed form & reselling risk").

# Related literature (theory)

Lai, Riezman, and Wang (2009): R&D unified, either upstream (with leakage), or downstream in single firm (higher cost), focus on decision to delegate or not.

Vencatachellum and Versaevel (2009): R&D unified, either upstream (with (dis)economies of scope), or in two competing firms, with spillovers, focus on choice to either delegate, cooperate, or compete, and welfare analysis.

Allain, Henry, and Kyle (2015): R part not considered, D may shift from upstream to downstream client, focus on effect of downstream competition.

# Related literature (empirical evidence)

Hagedoorn et al. (2012): above (below) a threshold of internal R&D, the marginal returns to internal R&D is higher (lower) when R&D is sourced externally, implying complements (substitutes).

Ceccagnoli et al. (2014): external and internal R&D neither complements nor substitutes (complementarity increases with prior licensing experience).

Higgins et al. (2006): firms with greater R&D intensity are more likely to engage in R&D outsourcing acquisitions.

Danzon et al. (2007): financially strong firms less likely to be part of acquisition, and a merger has little effect on R&D expenses.

# The model

One external for-profit lab (0):

$\mathbf{x} \doteq (x_1, x_2)$ external R&D

Two firms $(i, j = 1, 2)$:

$\mathbf{y} \doteq (y_1, y_2)$ internal R&D

$\mathbf{z} \doteq (z_1, z_2)$ commercial strategies

Firms compete (i) on the demand side of the intermediate R&D market, (ii) in internal R&D levels, (iii) on the final product market.

# The model

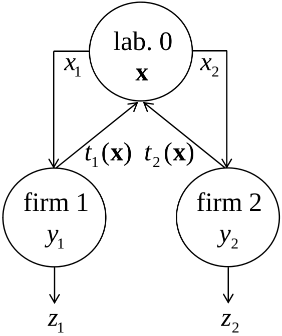


**Figure 1**: One lab (common agent) and two firms (principals)

which compete in external and internal R&D

and in the final product market

# The model

The lab's net profit:

$$v_0(\mathbf{x}) \doteq t_1(\mathbf{x}) + t_2(\mathbf{x}) - f_0(\mathbf{x})$$

Firm $i$'s net profit:

$$v_i(\mathbf{x}, \mathbf{y}, \mathbf{z}) \doteq g_i\left(x_i + y_i, x_j, y_j, \mathbf{z}\right) - f_i\left(y_i\right) - t_i(\mathbf{x})$$

$f_0$: lab's R&D cost of $\mathbf{x}$

$f_i$: firm $i$'s R&D cost function of $y_i$

$g_i$: firm $i$'s gross profit function of $\mathbf{x}, \mathbf{y}, \mathbf{z}$

$t_i$: firm $i$'s transfer payment function of $\mathbf{x}$

# The model

Timing:

(i) The firms choose non-cooperatively $t_i(\mathbf{x}) \geq 0$,

(ii) The lab contracts with both firms, only one, or none,

by choosing $\mathbf{x}$ to max $v_0(\mathbf{x})$ (i.e., given $t_i$ the lab contracts with firm $j$ only if

$$v_0(\mathbf{x}) \geq \sup\left\{0, \max_{\mathbf{x}}\{t_i(\mathbf{x}) - f_0(\mathbf{x})\}\right\}$$

for some $\mathbf{x} \geq (0, 0)$, $i = 1, 2, j \neq i$).

(iii) The firms choose non-cooperatively $y_i \geq 0$,

(iv) The firms choose non-cooperatively $z_i \geq 0$.

# The model

Notation:

$$\hat{g}_i\left(x_i + y_i, x_j, y_j\right) \doteq g_i\left(x_i + y_i, x_j, y_j, \mathbf{z}^*(\mathbf{x}, \mathbf{y})\right)$$

$$\tilde{g}_i\left(\mathbf{x}\right) \doteq \hat{g}_i(x_i + y_i^*(\mathbf{x}), x_j, y_j^*(\mathbf{x})) - f_i\left(y_i^*(\mathbf{x})\right)$$

By assumption:

Given $g_i$, for any $(\mathbf{x}, \mathbf{y})$ there exists a unique $\mathbf{z}^*(\mathbf{x}, \mathbf{y})$,

Given $\hat{g}_i$, for any $\mathbf{x}$ there exists a unique $\mathbf{y}^*(\mathbf{x})$.

# The model

Technological assumptions:

$$\frac{\partial \hat{g}_i}{\partial x_i} \geq \left\| \frac{\partial \hat{g}_i}{\partial x_j} \right\| \tag{1}$$

$$\| \qquad \qquad \bigvee\!|$$

$$\frac{\partial \hat{g}_i}{\partial y_i} \geq \left\| \frac{\partial \hat{g}_i}{\partial y_j} \right\| \tag{2}$$

and

$$\left\| \frac{\partial^2 \hat{g}_i}{\partial y_i \partial x_i} \right\| \geq \left\| \frac{\partial^2 \hat{g}_i}{\partial y_i \partial x_j} \right\| \tag{3}$$

$$\| \qquad \qquad \bigvee\!|$$

$$\left\| \frac{\partial^2 \hat{g}_i}{\partial y_i^2} \right\| \geq \left\| \frac{\partial^2 \hat{g}_i}{\partial y_i \partial y_j} \right\| \tag{4}$$

# External and internal R&D: complements or substitutes?

## Proposition 1

The equilibrium level of a firm's internal R&D activity $y_i^*$ is decreasing in the contracted external lab's activity $x_i$ if and only if the gross profit functions $\hat{g}_i$ have decreasing returns in $(x_i, y_i)$:

$$\frac{dy_i^*}{dx_i} \lesseqgtr 0 \Leftrightarrow \frac{\partial^2 \hat{g}_i}{\partial s_i^2} \lesseqgtr 0,$$

where $s_i \doteq x_i + y_i$, and $i = 1, 2$.[a]

[a] More specifically, $\frac{dy_i^*}{dx_i} = 0$ if and only if either (i) $\frac{\partial^2 \hat{g}_i}{\partial s_i^2} = 0$, or (ii) $\frac{\partial^2 \hat{g}_i}{\partial x_i^2} = \frac{\partial^2 \hat{g}_i}{\partial x_i \partial y_j} < 0$, $\frac{\partial^2 \hat{g}_j}{\partial x_j^2} = \frac{\partial^2 \hat{g}_j}{\partial x_j \partial x_j} < 0$, and $\frac{\partial^2 f_j}{\partial y_j^2} = 0$, where $i, j = 1, 2$, $j \neq i$.

# External and internal R&D: complements or substitutes?

1) internal and external operations are neither substitutes

nor complements *in general*,

2) second-order condition bears only on each firm $i$'s *own* argument $s_i$

not on $x_j$ or $y_j$, $i, j = 1, 2$, $i \neq j$,

3) unlike models of *horizontal* agreements where inter-firm spillovers drive

strategic complementarity/substitutability of R&D choices.

# Distribution of R&D benefits

Value function:

$$v\left(S\right) \doteq \max_{\mathbf{x}}\left(\sum_{i\in S}\tilde{g}_i\left(\mathbf{x}\right) - f_0(\mathbf{x})\right)$$

where $S \in \{\emptyset, \{1\}, \{2\}, \{1,2\}\}$, $v(\emptyset) = \underline{v}_0 = 0$ (normalization).

Aggregate measure of the two categories of externalities:

$$\epsilon \doteq v\left(\{1,2\}\right) - v\left(\{1\}\right) - v\left(\{2\}\right)$$

$$\epsilon = \begin{cases} \geq 0 & \text{positive externalities dominate} \\ < 0 & \text{negative externalities dominate} \end{cases}$$

# Distribution of R&D benefits

■ **Non-increasing returns to R&D**: Assume that $\frac{\partial^2 \hat{g}_i}{\partial s_i^2} \leq 0$.

*Non-negative R&D externalities.* Suppose that indirect and direct R&D externalities are non-negative:

$$\frac{\partial^2 f_0}{\partial x_i \partial x_j} \leq 0 \tag{5}$$

$$\frac{\partial \hat{g}_i}{\partial x_j} \geq 0 \quad \frac{\partial \hat{g}_i}{\partial y_j} \geq 0 \tag{6}$$

Characteristic of early-stage discovery with empirical evidence of economies of scope and significant knowledge spillovers (Henderson and Cockburn *RAND* 1996; Cockburn and Henderson *JHE* 2001)

# Distribution of R&D benefits

## Proposition 2

*Conditions* (**??**-**??**) *imply that* $\epsilon \geq 0$. *In all* TSPNE *there exists a continuum of firm payoffs* $(v_1^*, v_2^*) \geq (\underline{v}_1, \underline{v}_2)$ *that verify*

$$v_1^* + v_2^* = \Lambda, \tag{7}$$

*and the lab exactly breaks even, that is*

$$v_0^* = 0. \tag{8}$$

There is delinkage of incentives to invest in external unit from the value generated to exclusive benefit of downstream sponsors. Efficient projects at the industry level are vulnerable to upstream unfavorable events.

**Example** 1 (adapted from Symeonidis, *IJIO* 2003):

$p_i(q_i, q_j) = \left(1 - \frac{2q_i}{u_i^2} - \frac{q_j}{u_i u_j}\right)$, $i, j = 1, 2$, $j \neq i$, where $u_i$ is firm $i$'s product quality, which depends on R&D: $u_i = (s_i)^{\frac{1}{4}} + \beta (s_j)^{\frac{1}{4}}$, $\beta \in [0, 1]$ is a spillover parameter, $s_i \doteq x_i + y_i$ and $s_j \doteq x_j + y_j$. Set $\beta = \frac{1}{2}$, production costs to zero, and solve for Cournot-Nash quantities $q_1^*(x, y)$ and $q_2^*(x, y)$. Inserting the latter expressions in $g_i(s_i, x_j, y_j, \mathbf{q}) = p_i(q_i, q_j) q_i$ leads to $\hat{g}_i(s_i, x_j, y_j)$. We obtain $\frac{\partial^2 \hat{g}_i}{\partial s_i^2} < 0$ (decreasing returns) for all $s_i > 0$, so that from Proposition 1 we have $\frac{dy_i^*}{dx_i} < 0$ (R&D outsourcing reduces internal activity). Any additive cost function for the lab, e.g. $f_0(\mathbf{x}) = x_1 + x_2$, satisfies (**??**). Moreover $\frac{\partial \hat{g}_i}{\partial x_j} > 0$ and $\frac{\partial \hat{g}_i}{\partial y_j} > 0$ (positive direct externalities) for all $x_i, x_j > 0$, so that (**??**) is satisfied.

# Distribution of R&D benefits

*Negative R&D externalities.* Suppose that indirect and direct R&D externalities are negative:

$$\frac{\partial^2 f_0}{\partial x_i \partial x_j} > 0, \tag{9}$$

$$\frac{\partial \hat{g}_i}{\partial x_j} \leq 0, \quad \frac{\partial \hat{g}_i}{\partial y_j} \leq 0. \tag{10}$$

Characteristic of late-stage clinical trials with empirical evidence of diseconomies of scope and non-existent spillovers (Danzon et al., *JHE* 2005; Macher and Boerner, *SMJ* 2006).

# Distribution of R&D benefits

## Proposition 3

*Conditions* (**??**-**??**) *imply that* $\epsilon < 0$. *In all TSPNE there is a unique pair of firm payoffs* $(v_1^*, v_2^*)$ *that verify*

$$v_i^* = v(\{i\}) - |\epsilon| \geq \underline{v}_i, \tag{11}$$

$i, j = 1, 2$, $j \neq i$, *and the lab appropriates a share of industry profits*

$$v_0^* = |\epsilon| > 0. \tag{12}$$

The external unit can appropriates all profits in a buyers market where client firms are principals and are no less informed than the external unit.

**Example** 2 (adapted from Laussel and Le Breton, *JET* 2001):

$\mathbf{x}, \mathbf{y} \in \{0, 1\}^2$ and the lab's R&D costs are

$$f_0(\mathbf{x}) = \begin{cases} 1 & \text{if } x_1 + x_2 = 1 \\ 0 & \text{if } x_1 = x_2 = 0 \end{cases}$$

$f_0(\mathbf{x}) = +\infty$ otherwise, satisfying condition (**??**). Each firm's R&D cost is $f_i(y_i) = \gamma y_i$, with $\gamma \geq 1$, and production cost is $c_i(x_i + y_i)$, with $c_i(0) = c_H$ and $0 \leq c_i(1) = c_i(2) = c_L < c_H$. Total demand is $q = \sup\{0, a - p\}$, with $p \geq 0$ and $a > c_H$. Given $(\mathbf{x}, \mathbf{y})$, defining $\pi \doteq (c_H - c_L)(a - c_H)$, and solving for Bertrand-Nash equilibrium prices leads to $\hat{g}_i(x_i + y_i, x_j, y_j) = \pi > 0$ if $x_i + y_i \geq 1$ and $x_j + y_j = 0$, and $\hat{g}_i(x_i + y_i, x_j, y_j) = 0$ otherwise, so the condition in (**??**) is also satisfied. Equilibrium payoffs are $v_0^* = \pi - 1$, $v_i^* = v_j^* = \underline{v} = 0$.

# Distribution of R&D benefits

■ **Non-decreasing returns to R&D**. Assume that $\frac{\partial^2 \hat{g}_i}{\partial s_i^2} \geq 0$.

Simple sufficient conditions for Propositions 2 and 3 to remain valid:

**Proposition 4**

Suppose that returns to R&D are non-decreasing. Then Propositions 2 and 3 still hold if $\frac{\partial^2 \hat{g}_j}{\partial x_j \partial x_i} \geq 0$, $i, j = 1, 2$, $j \neq i$. Otherwise a sufficient condition is $\frac{dy_j^*}{dx_i} > -1$.

**Example** 4 (d'Aspremont and Jacquemin, *AER* 1988, & Vonortas *IJIO* 1994): $f_0(\mathbf{x}) = (x_1 + x_2)^2 - \frac{\delta}{2} x_1 x_2$, with $\delta \geq 0$, $f_i(y_i) = \kappa + y_i^2$, with $\kappa > 0$. Production cost is $c_i(\mathbf{x}) = (c - s_i - \beta s_j)$, with $c > 0$, with spillover parameter $\beta \in [0, 1]$, and where $s_i = x_i + y_i$. Inverse demand is $p(\mathbf{q}) = a - q_i - q_j$, so $q_i^*(\mathbf{x}, \mathbf{y}) = \left[(a - c) + s_i \left(2 - \beta\right) + s_j \left(2\beta - 1\right)\right] / 3$.

Then $\partial^2 \hat{g}_i / \partial s_i^2 = 2 \left(2 - \beta\right)^2 / 9 > 0$ (increasing returns to R&D), and:

(i) Proposition 2 applies if $\beta \geq 1/2$ *and* $\delta \geq 1$,

(ii) Proposition 3 applies if $\beta < 1/2$ and $\delta < 1$.

# Incentives to integrate

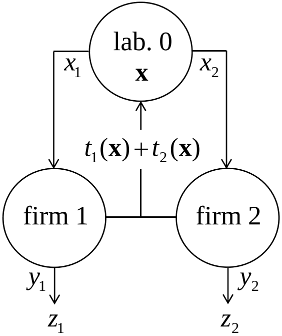


**Figure 2**: Inter-firm cooperation: joint R&D procurement

# Incentives to integrate

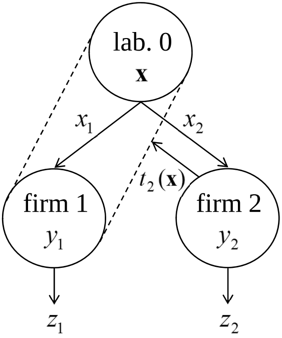


**Figure 3**: firm 1 and the lab integrate vertically

# Incentives to integrate

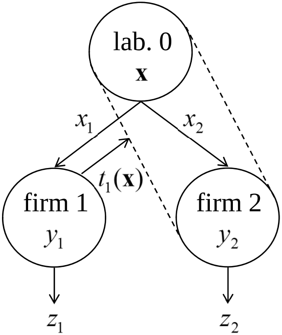


**Figure 4**: firm 2 and the lab integrate vertically

# Incentives to integrate

## ■ Non-negative R&D externalities ($\epsilon \geq 0$)

From Proposition 2: $v_0^* = 0$, and $v_1^* + v_2^* = \Lambda$ (where $v_i^* \geq \underline{v}_i$).

The payoff distribution $(v_1^*, v_2^*)$ reflects circumstances outside of the model specifications captured by bargaining powers $(\phi_1, \phi_2)$:

$$v_k^* = \underline{v}_k + \phi_k \left(\Lambda - \underline{v}\right),$$

$k = 1, 2$, where $(\underline{v}_1, \underline{v}_2)$ is the disagreement point, with $\underline{v} \doteq \underline{v}_1 + \underline{v}_2$ and $\phi_1 + \phi_2 = 1$. Then

$$\phi_k = \frac{v_k^* - \underline{v}_k}{\Lambda - \underline{v}}.$$

## Incentives to integrate

Suppose $v(\{i\}) > \underline{v}_i$. In case of vertical integration $\{0, i\}$:

$$v_{0+i}^{\{0,i\}} = v(\{i\}) + \phi_i \left(\Lambda - v(\{i\}) - \underline{v}_j\right) > v_i^*, \tag{13}$$

$$v_j^{\{0,i\}} = \underline{v}_j + \phi_j \left(\Lambda - v(\{i\}) - \underline{v}_j\right) < v_j^*. \tag{14}$$

From (**??**-**??**) willingness to pay for the lab simplifies to:

$$v_{0+i}^{\{0,i\}} - v_i^{\{0,j\}} = \phi_j \left(v(\{i\}) - \underline{v}_i\right) + \phi_i \left(v(\{j\}) - \underline{v}_j\right) > 0,$$

for a *strictly* higher payoff to the external unit than with outsourcing:

$$v_0^{\{0,1\}} = v_0^{\{0,2\}} = \frac{v(\{1\}) - \underline{v}_1}{\Lambda - \underline{v}} \left(v_2^* - \underline{v}_2\right) + \frac{v(\{2\}) - \underline{v}_2}{\Lambda - \underline{v}} \left(v_1^* - \underline{v}_1\right) > v_0^* = 0.$$

# Incentives to integrate

■ **Negative R&D externalities ($\epsilon < 0$)**

From Proposition 3: $v_0^* = |\epsilon| > 0$, and $v_i^* = v(\{i\}) - |\epsilon| \geq \underline{v}_i$.

In a horizontal arrangement for firms to behave as a unique principal:

$$v_0^{\{1,2\}} = 0, \qquad v_1^{\{1,2\}} + v_2^{\{1,2\}} = \Lambda,$$

and the two firms' payoffs $\left(v_1^{\{1,2\}}, v_2^{\{1,2\}}\right)$ verify:

$$v_k^{\{1,2\}} = v_k^* + \omega_k \left(\Lambda - v_1^* - v_2^*\right),$$

so bargaining powers are:

$$\omega_k = \frac{v_k^{\{1,2\}} - v_k^*}{\Lambda - v_1^* - v_2^*}.$$

...

# Incentives to integrate

The two firms' joint profit is maximized in the horizontal arrangement but each firm has an incentive to depart unilaterally from $1, 2$ by acquiring the external unit. The bidding process results in:

$$v_0^{\{0,1\}} = v_0^{\{0,2\}} = \frac{v\left(\{1\}\right) - \underline{v}_1}{|\epsilon|}\left(v_2^{\{1,2\}} - v_2^*\right) + \frac{v\left(\{2\}\right) - \underline{v}_2}{|\epsilon|}\left(v_1^{\{1,2\}} - v_1^*\right) \geq v_0^* = |\epsilon|\,.$$

With negative externalities the value extracted by the owners of the external unit in the equity market is only *weakly* superior to the positive outsourcing equilibrium payoff.

# Incentives to integrate

**Corollary 3**

From the viewpoint of the labs owners, incentives to participate in the equity market are weaker in the case of late-stage development (clinical trials) activities characterized by negative externalities, as compared with earlier-stage research (discovery).

Exit payoff results in a long-term financial incentive that motivates the foundation of a new research biotech (more than a development services provider).

# Appendix (1/2)

Definitions:

(1) for any $\mathbf{t} \doteq (t_1, t_2)$ the lab's profit-maximizing *R&D set* is

$X(\mathbf{t}) \doteq \arg\max_{\mathbf{x}} v_0(\mathbf{x}(\mathbf{t}))$

(2) for any $\mathbf{x} \in X(t_i, t_j)$ and $\mathbf{x}' \in X(t_i', t_j)$, firm $i$'s transfer function $t_i$ is *a best response* to the other firm's $t_j$ if $\tilde{g}_i(\mathbf{x}) - t_i(\mathbf{x}) \geq \tilde{g}_i(\mathbf{x}') - t_i'(\mathbf{x}')$, all $t_i'$

(3) the transfer function $t_i$ is *truthful* relative to $\tilde{\mathbf{x}}$ if

$t_i(\mathbf{x}) \doteq \sup\{0, \tilde{g}_i(\mathbf{x}) - (\tilde{g}_i(\tilde{\mathbf{x}}) - t_i(\tilde{\mathbf{x}}))\}$

# Appendix (2/2)

Equilibrium concept:

$(\tilde{\mathbf{t}}, \tilde{\mathbf{x}}, \tilde{\mathbf{y}}, \tilde{\mathbf{z}})$ is a Truthful Subgame-Perfect Nash Equilibrium (TSPNE) if:

- $(i)$ $\tilde{\mathbf{z}} = \mathbf{z}^*(\tilde{\mathbf{x}}, \tilde{\mathbf{y}})$
- $(ii)$ $\tilde{\mathbf{y}} = \mathbf{y}^*(\tilde{\mathbf{x}})$
- $(iii)$ $\tilde{\mathbf{x}} \in X(\tilde{\mathbf{t}})$
- $(iv)$ $\tilde{t}_i$ is a best response to $\tilde{t}_j$
- $(v)$ $\tilde{t}_i$ is truthful relative to $\tilde{\mathbf{x}}$

$\tilde{t}_i(\mathbf{x}) = \sup\{0, \tilde{g}_i(\mathbf{x}) - v_i^*\}$, where $v_i^* \doteq \tilde{g}_i(\tilde{\mathbf{x}}) - \tilde{t}_i(\tilde{\mathbf{x}})$ is firm $i$'s net equilibrium payoff