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One Lab, Two Firms, Many Possibilities: on R&D outsourcing in the biopharmaceutical industry

Etienne Billette de Villemeur and Bruno Versaevel

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on R&D outsourcing in the biopharmaceutical industry

Etienne Billette de Villemeur[*]   Bruno Versaevel[†]

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Abstract

We draw from documented characteristics of the biopharmaceutical industry to construct a model where two firms can choose to outsource R&D to an external unit, and/or engage in internal R&D, before competing in a final market. We investigate the tension between internal and outsourced operations, the distribution of profits among market participants, and the incentives to coordinate outsourcing activities or to integrate R&D and production. Consistent with the empirical evidence, we find that: (i) internal and external operations are neither substitutes nor complements in general, as each firm's in-house effort level can be reduced or stimulated by the external unit's activities, depending on the nature of R&D returns; (ii) an aggregate measure of technological externalities drives the distribution of industry profits, with higher returns to the external unit for development (clinical trials) than for research (drug discovery); (iii) in the latter case, the delinkage of investment incentives from industry value, and the vulnerability of investors' returns to negative shocks, both suggest the abandonment of projects with economic and medical value as a likely consequence of outsourcing; (iv) upstream entry is stimulated by the long-run perspective for founders of a research biotech, more than of a clinical services unit, to extract – or reappropriate – industry profits by selling the equity to a client firm.

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[*]Université de Lille & LEM (CNRS), France.
[†]EMLYON business school & GATE (CNRS), France. Corresponding author (versaevel@em-lyon.com).

1   Introduction

There is evidence that pharmaceutical firms that engage in internal R&D (research and development) increasingly outsource specific tasks. Morton and Kyle (2012) report a worldwide compound annual growth rate of 16.6% in contract R&D, with expenses rising from US$ 14 billion in 2003 to 47 billion in 2011. This trend is viewed as an attempt to reverse a decline in R&D productivity observed over several decades (Munos, 2009; Pammolli et al., 2011; Mestre-Ferrandiz et al., 2012).

While the number of new molecular entities and biologics that are approved annually by the US Food and Drug Administration (FDA) has remained around the same level since 1950, when measured per billion US dollars spent on R&D this number has halved roughly every 9 years (Scannell et al., 2012). Although the reasons for this long-term decline are multiple, industry experts point to technological challenges as a key driver of the rise in R&D costs. The scale of the productivity problem can be gauged by considering changes in the average full cost estimate of bringing a new compound to the market. This estimate is $451 million in DiMasi et al. (1991), $1,031 million in DiMasi et al. (2013), and $2,558 million in DiMasi et al. (2016).[1] Despite this cost escalation, as gross margins have evolved in parallel with R&D spending (Scherer, 2001, 2010), the net profit returns have remained persistently high at the aggregated industry level.

It is believed in the industry that R&D outsourcing can reduce costs by increasing efficiency in the discovery and testing steps toward new medicines (Schuhmacher et al., 2016). The tasks that firms choose to contract out cover a large spectrum of activities, from basic research to late-stage development, including genetic engineering, target validation, assay development, safety and efficacy tests in animal models, and clinical trials involving human subjects. At the same time, large pharmaceutical firms invest large amounts of financial resources to acquire specialized innovative units involved in promising projects. For example, in the oncology domain, AbbVie agreed to buy Pharmacyclics for $21 billion in 2015, and Pfizer acquired Medivation for $14 billion in 2016. Some of the targets are also involved in clinical trials, like Medarex which evolved from a research entity to a development company before Bristol-Myers Squibb acquired it for $2.4 billion in 2009. Such acquisitions are viewed by industry leaders as another response to the declining R&D productivity problem

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[1]Here we focus on estimates based on the same methodology to estimate costs, which include out-of-pocket R&D costs and time cost (i.e., cost of capital). The estimate in DiMasi et al. (2016) is in 2013 prices, and the cost estimates in DiMasi et al. (1991, 2003) have been updated to US$ 2011 prices in Mestre-Ferrandiz et al. (2012). The latter paper offers a detailed discussion on the approaches used to estimate the full cost of bringing a new compound to the market.

(Comanor and Scherer, 2013). The absorption of an independent specialized unit by a pharmaceutical firm substitutes for a contractual relation between the two entities, and the two technology outsourcing alternatives amount to R&D expenditures. Still the high transaction prices observed in the equity market suggest that pharmaceutical firms pay more for R&D by acquiring an external unit than by contracting with it as a client firm, or by carrying out the R&D internally (Pisano, 2015).

Over the past two decades, a growing stream of economics literature – which we review below – has investigated a variety of issues that pertain to R&D outsourcing. However, most theoretical contributions adopt a general approach without specific reference to the particularities of the bio-pharmaceutical sector, and several empirical analyses offer mixed results that leave important questions unanswered. Does R&D outsourcing necessarily coincide with a disinvestment of big pharma firms from internal drug discovery or clinical trial activities? Can technological characteristics of contracted-out operations, and the nature of the R&D tasks, explain the low average profitability of biotech units that engage in basic research, or the higher financial returns of contract research organizations involved in later-stage development? Do big pharma firms effectively pay more for R&D by acquiring an external unit than by contracting with it? From the viewpoint of the external unit's owners, do incentives to participate in the equity market depend on the nature of R&D activities?

In order to answer these questions, we draw on documented characteristics of the biopharmaceutical industry to construct a model in which a for-profit independent unit (e.g., a biotech startup, or a contract research organization) conducts specific tasks as solicited non-cooperatively by two firms (big pharma), which also run R&D operations internally, before competing in a final market. The external unit interacts with the two firms by responding to their contractual offers, and can choose to serve both firms, only one, or none. The firms can substitute internal resources for some or all of the external unit's operations, and their contractual offers reflect multi-stage strategic interactions in the intermediate R&D market and in the final product market. Incentives to pay for outsourced R&D depend on the exact effects of the received technology, and of the related internal R&D, on the firms' respective cost and demand conditions. The model allows us (i) to determine whether outsourced and in-house R&D perform as complements or rather as substitutes, then (ii) to identify technological drivers of the distribution of profits among the external unit and its sponsors, and (iii) to characterize the incentives for the client firms, and the payoff consequences for the upstream investors, to integrate R&D and production vertically, or to opt for other organizational arrangements.

Overall, the formal analysis leads to new insights on the functioning of R&D outsourcing and its implications for biopharmaceutical firms and their external partners, with strong and intelligible connections to the recent empirical evidence on the relation between contracted-out and in-house technological activities, on the nature of knowledge externalities in discovery and clinical development, and on merger activity in the equity market.

More specifically, our model produces three sets of results. First, we characterize the circumstances in which outsourced R&D either stimulates or reduces the internal R&D levels (Proposition 1). This is made possible by the specification that, unlike the models that we know in the theoretical R&D literature, the choices by the external unit, and by the firms on the demand side of the market for technology, are not *a priori* complementary or substitutable. We find that each firm's equilibrium internal effort level increases or decreases with the R&D sourced from the external unit, and that the sign of the relationship does not depend on technological spillovers. More specifically, a firm's internal effort decreases in the outsourced R&D if and only if the gross profits (before incurring R&D costs) have decreasing returns to the same firm's own R&D (i.e., the R&D that it specifically buys from the external unit or that it runs internally). This theoretical characterization echoes the most recent empirical investigations (e.g., Hagedoorn and Wang, 2012; Ceccagnoli, Higgins, and Palermo, 2014) that show that external and internal R&D, in the biopharmaceutical industry, are neither complements nor substitutes in general, as the exact connection between the two channels is rooted in complex specifications that differ across the set of examined cases.

Second, we establish simple conditions on the model primitives for the total equilibrium R&D benefits to be either fully appropriated by the two firms, or partially retained by the external unit. These conditions relate to the sign and respective magnitudes of indirect and direct technological externalities, and can explain the persistently low average profitability of biotech firms (Pisano, 2006, 2010). There are *indirect* technological externalities if the cost of R&D, as conducted by the external unit for the two firms, reflects economies or diseconomies of scope. There are *direct* technological externalities if some of the R&D received or produced by a firm impacts the gross profit of its competitor. Our conditions notably establish that the external unit exactly breaks even (for a zero economic profit) when the indirect (through the external unit) and direct (inter-firm) externalities are positive (Proposition 2). This first theoretical situation receives empirical support from several investigations that find evidence of economies of scope and significant knowledge spillovers in early-stage

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discovery activities (Henderson and Cockburn, 1996; Cockburn and Henderson, 2001; Bloom et al., 2013) on which biotech units focus. This case thus describes circumstances where outsourcing can reduce the costs of discovering new medicines but still, where investors have no positive incentive to engage financial resources. And this occurs precisely for the research tasks of the most fundamental nature. The risks involved in such technological uncertainties make this situation of market failure even more problematic. In our model, the contractual transfer payments in fact protect the client firms from the risk inherent to upstream operations (we illustrate this feature with specific functional forms in several examples). With an expected payoff exactly equal to zero in equilibrium, an unfavorable draw in the distribution implies a negative return and leads the external unit to shut down, although its activities generate a positive – and possibly very high – profit at the industry level. This outcome suggests that protection measures for the external unit (e.g., the financial back-up of a partner university) are necessary to avoid the abandonment of socially valuable research projects.

However, in our model the external unit can also appropriate a positive share – that can be derived analytically – of total profits when the externalities are negative, in which case the client firms earn only their marginal contribution to the industry profits (Proposition 3). This second situation is consistent with the empirical studies that identify diseconomies of scope and nonexistent spillovers in the late-phase clinical trials of candidate drugs (Danzon et al. 2005; Macher and Boerner, 2006), such as conducted by specialized contract research organizations (see section 2). In that case the profits to the external unit are an effect of competition between the contract offers of the two firms for the orientation of R&D resources toward specific needs. The intensity of that competition depends on the nature of the R&D activities, both inside the external unit and in the firms' internal facilities, and then on the effect of such activities on the downstream cost and demand characteristics, which in the end also impact final market interactions.

From these results emerge unambiguous connections between the nature of research and (distinctively) development activities with the sign of technological externalities and with the distribution of profits among participants in the market for R&D market. These connections allow us to identify circumstances where incentives to invest in the external unit are delinked from the value generated to the exclusive benefit of downstream sponsors (Corollary 1), and where efficient projects at the industry level are vulnerable to unfavorable technological events (Corollary 2). Such circumstances suggest the abandonment of projects with economic and medical value as a likely consequence of R&D

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outsourcing, and lead us to put in perspective the widespread belief, among business profession-als in the biopharmaceutical industry, that the externalization of discovery and clinical development activities can only contribute to solving the R&D productivity issue.

A third set of results connects the technological conditions that drive the distribution of R&D benefits to the firms' incentives to participate in the equity market. We identify two categories of cases that depend on the ability of firms to bid or not for the external unit, depending on financial, managerial, or governance constraints of all kinds. If such constraints are binding, either positive technological externalities dominate and the firms remain independent, or negative externalities lead the firms to choose to coordinate horizontally their R&D outsourcing (as in Majewski, 2004). Other-wise, should the firms be unable to commit to *not* unilaterally considering vertical integration, one of them does acquire the external unit. Whether one or the other firm is the acquirer occurs with equiprobability, independently of firm asymmetries. The main outcome is that the competition for the control of the external unit leads to overbidding (a case discussed in Higgins and Rodriguez, 2006), although the premium can be nil in the case of negative externalities (diseconomies of scope and inexistant inter-firm spillovers), as characteristic of late-stage development tasks (Proposition 6). We thus obtain that principally biotech founders engaged in early-stage research reappropriate in the equity market part of the value transferred to their sponsors in the R&D market (Corollary 3).

Our model specifications depart from those of recent theoretical papers where research and de-velopment operations are not considered separately, but are viewed as a single activity that is fully performed either by an external unit or, exclusively so, internally by a firm. In Lai, Riezman, and Wang (2009), a single client firm (a principal) offers a contract to the external unit (an agent), al-though some technological information can be leaked subsequently to a competitor. When writing the contract, the firm trades-off between the benefit of the external unit's superior R&D efficiency and the revenue loss caused by the leakage. For some parameter values, the firm finds it profitable to externalize R&D with a lump-sum contract even though this allows the leakage to occur. In Ho (2009), after the external unit accepts the contract and incurs the fixed cost, if successful then it can secretly offer the technology to a final-market competitor of the principal for a higher total revenue, before reporting a failure to the outsourcing firm. Any contract that incentivizes the external unit not to leak the technology it shown to necessarily result in a lower net profit to the principal than the status quo (no outsourcing).

R&D operations are also formalized as a single activity in Vencatachellum and Versaevel (2009), although we share with the latter contribution the focus on the strategic interactions of two firms (principals), which simultaneously offer competing contracts to an external unit (a common agency situation). An observable "active" leakage occurs when the contracts incentivize the external unit to serve both firms, together with a "passive" (unsolicited) leakage captured by an inter-firm spillover parameter. As a result, with positive economies of scope, but limited spillovers, the two firms receive specific R&D services and earn higher equilibrium profits than by relying on internal resources.

Complete information also excludes secret reselling in Spulber (2013), where a set of competing external inventors – or a multiproject monopoly inventor – engage in uncertain R&D projects for a new production technology. After the R&D takes place upstream, client firms observe the inventions together with their respective inventors' two-part royalty offers, and simultaneously make adoption and product pricing decisions. In equilibrium, all firms adopt the most efficient technology. When the downstream firms vertically integrate R&D and production operations – a possibility also considered in our model – and agree to share the best invention obtained from all projects before competing in prices in the final market, the R&D activity is suboptimal.

A important specification of our model is that a vertical division of labour in R&D activities may occur, like in Allain, Henry, and Kyle (2015) where an external research unit, which generates new technology of uncertain value, faces a set of potential client firms which compete in an auction for the exclusive benefit of the technology. When the research unit is *ex ante* more confident about the value of the innovation than the firms, it chooses to develop it on its own for a higher expected benefit if and only if its cost disadvantage is not too large. The latter situation is more likely if, following an increase in the number of firms, the positive effect on the license fee resulting from the auction (more bidders participate) dominates the negative effect on gross profits (more downstream competition).[2]

We share with Spulber (2013) and Allain et al. (2015) the assumption that complete information or property rights prevent secret reselling, together with the characterization of the connection between the nature of competition among client firms and incentives to engage in R&D operations. Our approach is complementary to both contributions, where the intensity of downstream competition is driven by the number of client firms. In our model, the number of firms on the demand side of the R&D market is constant, and the intensity of competition is a consequence of the exact effects

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[2]Allain et al. (2015) also construct a large dataset on exclusive licensing deals and investigate the drivers of the decision, by a research unit that has discovered a drug candidate, to proceed also to development operations.

of external and internal R&D operations on cost and demand conditions. As in Allain et al. (2015), the intensity of competition among client firms drives the vertical division of labor in R&D operations, and as in Spulber (2013) an appropriability problem may lead to integrate R&D and production vertically. We also share with Ho (2009), Lai, Riezman, and Wang (2009) and Vencatachellum and Versaevel (2009) the assumption that the firms write contract offers, to which the external unit responds, and which can lead to multi-contracting. A key specific feature of our model, consistently with the biopharmaceutical context, is that the firms, which also run internal research and/or development tasks, condition their payments on a measure of the external unit's operations, formalizing some kind of dialogue in the market for technology (so the external unit's operations are *not* conducted *before* the client firms' choice of payment schemes).

Our formal analysis also connects to the empirical evidence on the organization of R&D in the biopharmaceutical industry. The endogeneity of the respective efforts of the external unit and its client firms, in our model, captures the observation that the distribution of tasks between a specialized R&D supplier and its sponsors might vary significantly on a case by case basis. Recent results appear notably in Hagedoorn and Wang (2012), where a panel sample of incumbent pharmaceutical firms is used, with the innovative output (the dependent variable) measured as the number of annual biotechnology patents granted to these firms. The level of internal R&D expenditure is found to drive the interactive effect between external and internal R&D strategies. Above (below) a threshold level of internal R&D investments, the marginal returns to internal R&D are higher (lower) when new technology is sourced externally through alliances or acquisitions, which indicates complementarity (substitutability). An ambiguous conclusion is also reached in Ceccagnoli, Higgins, and Palermo (2014), where another panel dataset from the biopharmaceutical industry is used to estimate the partial cross-derivative of an innovation production function (the output is the yearly stock of compounds in a firm's pipeline) with respect to external (in-licensing) and internal R&D expenditure. The results suggest that external and internal R&D are neither complements nor substitutes, and that complementarity increases with a few drivers (e.g., prior licensing experience). Our first formal proposition, in Section 4, accords with these empirical results.[3]

Another set of papers use data collected at the firm level and at the level of individual R&D

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[3]Papers such as Veugelers and Cassiman (1999, 2005), and Cassiman and Veugelers (2006) find similar results by using cross-sectional data on R&D active firms, and conclude that the complementarity between external and internal sources of technology is context related.

projects in order to distinguish between economies of scale and economies of scope in the production of intellectual property. The evidence depends on the nature of technological activities. Henderson and Cockburn (1996), Cockburn and Henderson (2001), and Bloom, Schankerman, and Van Reenen (2013) find economies of scope and significant knowledge spillovers in early-stage drug "discovery" tasks (those on with biotech units typically focus). However, Danzon, Nicholson, and Sousa Pereira (2005), and Macher and Boerner (2006), identify diseconomies of scope and nonexistent spillovers in the late-phase clinical trials of candidate medicines (the "development" activities that are usually outsourced to specialized CROs). Two of our theoretical propositions, in Section 4, clearly echo these contrasted empirical results, and show their relevance for explaining the distribution of industry profits between an external unit and its client firms.

A few other recent papers point to the ability of client firms, in the biopharmaceutical industry, to contractually control the behavior of external technology suppliers. Robinson and Stuart (2007) study the features of early-stage (discovery) research contractual agreements, in which large firms sponsor small biotech companies. Their results suggest that a client firm can obtain broader termination rights when provisions on unverifiable research decisions are included in a contract, and thus enhance the *ex ante* incentives of the external research unit to uphold the contract. Higgins (2007) also analyzes R&D alliances between a firm and a biotech company. The milestone payment structure, in 90 percent of the contracts, is found to protect the client firm from misbehavior by conditioning financing on clearly identified objectives. Lerner and Malmendier (2010) examine agreements that involve a biotech firm as an R&D provider. They find that termination rights, which are assigned to the financing firm in 96 percent of the contracts, incentivize the subcontractor to remain focused on the objectives specified in the agreement.[4] The fine tuning of the client firms' payments with the operations of the external unit in our model is consistent with these conclusions.

Another set of papers focuses on the drivers or implications of mergers and acquisitions in the pharma industry. Higgins and Rodriguez (2006) examine the performance of acquisitions by established pharmaceutical firms of smaller competitors and/or biotech units to understand the effect of R&D outsourcing acquisitions on an individual firm's R&D productivity. They notably find that acquisitions supplement a firm's internal R&D efforts, and that firms with greater R&D intensity are

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[4]In a model that precedes their empirical analysis, Lerner and Malmendier (2010) show that if the R&D supplier is not financially constrained, the termination rights coupled with transfer payments can result in the same outcome as a simple complete contract.

more likely to engage in acquisitions. Danzon, Epstein, and Nicholson (2007) examine the determinants and effects of a sample of operations that include the purchase by pharmaceutical firms of an equity stake in biotech firms. They find in particular that financially strong firms are less likely to be part of an acquisition, either as a target or as an acquirer. We use these findings to comment our results in Section 5.

The paper is organized as follows. Characteristics of the biopharmaceutical industry are presented in Section 2, in connection to the model specifications introduced in Section 3. The interplay of outsourced and internal endogenous R&D levels, and the distribution of industry profits, are both characterized in Section 4. Incentives to shift to a more integrated industry structure are investigated in Section 5. Final remarks are in Section 6.

2   The Industry Context

We derive our theoretical results from model specifications that are carefully related to documented characteristics of the biopharmaceutical "market for technology" (Arora et al., 2001, 2004), where the industry usually divides research and development activities into two sets. The early-stage research ("R") consists in the discovery of new chemical compounds, vaccine candidates, or other biologics. The later-stage development ("D") tasks aim at assessing the safety and efficacy of the therapeutic or prophylactic properties of a candidate medicine on increasingly large populations of individuals. This stage moves toward the approval of a drug or the licensure of a vaccine by a government agency.

Outsourced R&D activities include early-stage research in the biotechnology field, where from the early years onward,

> "[b]ecause different commercial products were based on similar basic technologies, the costs ... could be shared by clients" (Pisano, 1991, p. 241) and then "[v]irtually every new entrant ... formed at least one, and usually several, contractual relationships with established pharmaceutical (and sometimes chemical) companies" (Pisano, 2006, p. 87).[5]

A well-documented case is the multi-year collaboration initiated by Merck and Sandoz with

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[5]According to Higgins (2007), who uses a large data set of alliances in the biopharmaceutical industry, from 1994 to 2001 each biotechnology firms had on average six alliance partnerships with large pharmaceutical firms.

Repligen in 1987 and 1989, respectively, for HIV therapeutics.[6] A more recent case involves Cure-Vac, which contracted with Johnson & Johnson in 2013, and with Sanofi in 2014, for the development of prophylactic vaccines. Another example involves Moderna Therapeutics, which in 2016 partnered with AstraZeneca, and a few months later with Merck, to develop RNA-based candidates for the treatment or prevention of a range of cancers. Accordingly, in our model an external unit can serve up to two client firms simultaneously.

Another important characteristic of the current market for biotechnology is that established pharmaceutical firms do not only give a biotech firm (external unit) access to finance and to manufacturing or marketing resources, they also operate internal biotechnology functions. The situation was different when the biotechnology market emerged in the mid-1970s. At that time there was a clear dichotomy in the R&D focus of suppliers and buyers. On the supply side, a typical new biotech firm used advances in cell and molecular biology for the design of a new therapeutic agent (e.g., a protein). On the demand side, the established pharmaceutical firms, whose technological competence focused on the random screening of compounds against disease targets, procured research in the market for biotechnology before engaging in clinical development. Since then, the largest pharmaceutical firms have acquired capabilities in molecular genetics and recombinant DNA technology (Galambos and Sturchio, 1998), so that the dichotomy has eroded:

> "[e]stablished firms have embraced biological approaches, including genomics, to drug discovery, while 'biotech firms' employ chemistry" (Pisano, 2006; p. 17). In other words, "[a]lthough the general trend toward increasingly outsourcing what was formerly in-house research is there for all to see, 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; p. 56).

Outsourced R&D also relates to late-stage development activities. Once a new compound, or a candidate vaccine, has been discovered, and tested in animal models, it must go through clinical trials conducted on human subjects. These trials need to produce evidence of safety and efficacy, as required for regulatory approval by government agencies (e.g., the FDA) before market introduction. There are three phases that involve increasingly large samples of subjects from a few dozen (phase 1) to, in case of success, several hundred (phase 2), and then to several thousand subjects (phase 3).

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[6]For a case study see Bower and Whittaker (1993).

Industry studies show persistent growth worldwide in the proportion of expenditures for clinical trials outsourced to specialized contract research organizations (CROs), from 26% in 2003 to 38% in 2010 (Aldrich, 2012), for higher financial returns than in the case of early-stage activities.[7] As in the case of biotechs, a subcontractor of clinical trial services forms simultaneous contractual relationships with several clients. In 2011, for example, Parexel entered into multi-year contractual agreements with both Merck and Pfizer. The contracting firms do not restrict their strategies to either make or buy clinical trial services as "[f]or a given study, sponsors can choose to retain some functions in house while contracting out others" (Azoulay, 2004; p. 1594). By outsourcing the latter tasks the firms attempt to benefit from economies of scale and scope (Macher and Boerner, 2006), and thereby to reduce their clinical trial costs, which are estimated at around US$220 million for a new drug (Mestre-Ferrandiz, Sussex, and Towse, 2012).[8]

In our model, the respective efforts of the external unit and its client firms are endogenous, so that the vertical division of R&D activities can occur at any point between total outsourcing and full integration. This specification is consistent with the observation that the collaboration of big pharma firms with biotech units or clinical trial providers creates joint inputs across the two sides of the contractual relationship, with an exact balance that might vary significantly on a case by case basis.

At all stages of the R&D process, the demand side usually designs the contracts that organize a technological relationship. This is explained by the fact that, when internal resources are available, the capacity of established pharmaceutical firms to "go for it alone" – though possibly at a higher cost – increases their bargaining power (Arora et al., 2004). Other factors include the severe financial constraints faced by specialized biotech units (Lerner and Merges, 1998; Golec and Vernon, 2009), together with a high rate of entry on the supply side (Rothaermel, 2001; Argyres and Liebeskind, 2002) while incumbents on the demand side remain highly concentrated. Although the latter structural features describe a "buyer's market", we show that they cannot fully explain the persistently low average profitability of biotech firms since the late 1970s (Pisano, 2006, 2010).[9] Indeed, in the anal-

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[7]For example, business experts observe that "[t]he robust fundamental drivers fuelling CRO market growth and consolidation have, for a number of years, also attracted the attention of private equity investors and, more recently, the capital markets. (...) Key features that make this growth segment of the healthcare industry particularly attractive to private investors seeking to realise high annual returns and exits within 3-5 years include: high visibility of revenues, excess cash generation, strong balance sheets and limited exposure to a number of risks that commonly affect biopharma companies (...)" (Bali, de Lima, and Yang, Results Healthcare, http://resultshealthcare.com, 2013.)

[8]The out-of-pocket cost of clinical testing depends on the number of patients required to collect sufficient data as demanded from regulatory agencies. It is even higher in the case of preventive vaccine candidates, as the size of human subject test samples is often larger than for drugs (Scherer, 2011; Keith et al., 2013).

[9]Over the last years the average profitability of biotech companies has remained low: "Of the 286 biotech companies

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ysis that follows we identify circumstances where the external unit appropriates the total industry profit, for any probability of R&D success, with client firms that behave as principals and are no less informed than the common independent contractor.

Detailed studies of R&D agreements find that contracts incorporate complex clauses to fine tune the financial mechanism (equity participation, milestone payments, licensing fees, ...) with the technology supplied (or not) by the external unit to other possible client firms. Non-compete clauses delineate the know-how that the external unit may not use with a third party, except as expressly authorized. Such clauses typically include a "right of first refusal" (Folta, 1998; Hagedoorn and Hesen, 2007) that allows a firm to purchase the rights – or only a selection – to the R&D outcomes of a biotech supplier before such an option is offered to third parties. Other clauses introduce a "right to match offer", whereby the external unit commits contractually to notify the client firm of its intent to contract with another party, and thereby to reveal the technological and financial terms of the competing offer (e.g., the amount and timing of any milestone payments).[10] Such clauses thus form a contractual link between the payments received by the external unit from a client firm and the technology that can be supplied to a competitor. Accordingly, in our model each firm can condition its payment scheme on the verifiable operations that are conducted inside the external unit, including those that relate to a third party. This assumption does not mean that a technology received from the external unit cannot partly benefit a competitor. Unsolicited and non contractible technological spillovers, both through the external unit and across firms, are introduced in the analysis.

Several theoretical analyses in the literature, with no reference to a particular industry (see the introduction), specify a research unit that is more knowledgeable than its client firms[11], or that can contract secretly with competitors. In the biopharmaceutical context, secret reselling is unlikely when biotech firms and clinical trial suppliers alike enhance their reputation by communicating on their contractual partners and on the content of agreements.[12] We thus choose to investigate a comple-

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trading on public exchanges today, 241 focus on drug development, a slight drop in numbers from last year. Of these 241 in the biopharmaceutical space, only 28 (12%) had both a product on the market and positive net income for FY 2012."(D. Thomas, Inside Bio Industry Analysis, http://www.biotech-now.org, 05/16/2013.)

[10]For example, non-compete clauses of this kind appear in contractual agreements between Merck and Tularik (dated Dec. 22, 1996), and between Eli Lilly and the same biotech company (Sep. 24, 1999). The contracts are available at: http://contracts.onecle.com/alpha

[11]In theoretical models of R&D with asymmetric information, the innovator, usually specified as an agent, is assumed to be better informed than a firm, specified as a principal. Such an assumption captures circumstances where, for example, a biotech has accumulated more knowledge on the value of a project than its downstream industrial partners. However, in many other circumstances, pharma firms that conduct R&D operations internally can also be more informed on the technological potential of a research program than a CRO that performs systematic tests on lead products candidates.

[12]Moreover, "the identities of partners and descriptions of alliances figure prominently in biotechnology companies'

mentary approach where client firms, which can engage in research and development operations, are not less competent than an external unit, and are not threatened by some form of misbehavior. Uncertainty, in our model, is a risk of failure in technological activities, as conducted externally or internally, or in downstream commercial operations, that is faced by all parties, without assuming superior information on the supply side of the R&D market. This approach is motivated by well-documented observations in science-based businesses:

> "Uncertainty related to the success/failure of R&D activities is the major concern for R&D managers in the biopharmaceutical industry. If the R&D activity is unsuccessful, indeed, there is no product to commercialize." (Pennings and Sereno, 2011; p. 375).

Our model specifications are consistent with early-stage (research) and phase 1 clinical trial (development) activities, when the outcomes of operations are *a priori* uncertain to all parties.[13] In any case, for all drugs, vaccines, or other biologics, contracting problems in later-stage alliances are also limited if "contingencies can be readily specified and outcomes are subject to external validation" (Robinson and Stuart, 2007; p. 7), for example when "the biotechnology researchers have to perform specifiable experiments on a lead product candidate" (Lerner and Malmendier, 2010; p. 215).

Finally, big pharma firms also take part in the equity market to acquire external R&D units. Recent examples include Merck taking control of Idenix (antiviral therapeutics) in 2014, AstraZeneca of Acerta Pharma (oncology and autoimmune diseases) and AbbVie of Pharmacyclics (immune-related disorders) in 2015. Acquisitions usually conclude a bidding contest where several big pharma rivals vie for the same buyout target.[14] Accordingly, in our model we assume that the firms' owners can bid for the control of the external unit, and assess the claim by industry experts that equity valuations are often excessive.[15]

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securities registration statements" when an initial public offering is in preparation (Stuart et al., 1999, p. 327; see also Baum, Calabrese, Silverman, 2000), and government agencies scrutinize all the steps before possible market introduction and public authorization.

[13]The specification that an agent in charge of an innovation project with uncertain payoff has no superior information *before* acting than its client firms can be seen as "a reasonable assumption if we are at the initial stages of a research undertaking" (Holmström, 1989; p. 310).

[14]"For several days, Johnson & Johnson was considered the most likely acquirer of Pharmacyclics, and there were erroneous news reports on Wednesday before the markets closed that it had won the bidding. But AbbVie stepped in with a higher bid ..." (www.nytimes.com, March 5, 2015); or "AstraZeneca Plc and Pfizer Inc. are among firms considering a counteroffer for Medivation Inc., challenging Sanofi's $9.3 billion bid for the company ..." (www.bloomberg.com, April 29, 2016).

[15]"AbbVie shares were down 3% in Thursday trading, as some investors and analysts expressed concern the company was overpaying for Pharmacyclics, of Sunnyvale, Calif, which sells a drug called Imbruvica with partner Johnson & Johnson." (www.wsj.com, May 5, 2015); and "GlaxoSmithKline CEO Andrew Witty questioned the ... valuations of recent deals" ... and stated that "[s]ome of these valuations look stretched." (www.firstwordpharma.com, May 11, 2015).

3 The Model

In this section we draw on the industry characteristics described above to construct a formal model. There are two related research and development (R&D) stages in an intermediate market for technology, and a final product market. Upstream, a for-profit independent unit (hereafter, "the lab") supplies new technology.[16] Downstream, two firms can outsource R&D to the lab, and/or conduct in-house R&D operations, before competing in the final market, where they supply substitutable (possibly imperfectly so) goods.

Profit functions — The non-negative *external* R&D levels, as chosen by the lab specifically for each firm, are described by $\mathbf{x} \doteq (x_1, x_2)$. The *internal* R&D levels, as chosen by the two firms, are described by $\mathbf{y} \doteq (y_1, y_2)$. The final-market strategies are denoted by $\mathbf{z} \doteq (z_1, z_2)$.[17]

The lab's net profit is

$$v_0(\mathbf{x}) \doteq t_1(\mathbf{x}) + t_2(\mathbf{x}) - f_0(\mathbf{x}), \tag{1}$$

where f_0 is the lab's cost, and t_i is firm i's transfer payment, both functions of $\mathbf{x}$. In line with the stylized facts described in section 2, the latter transfer function formalizes the fine tuning of firms' payments with the verifiable operations inside the external unit, as made possible by complex non-compete contractual clauses.[18]

Each firm i's net profit is

$$v_i(\mathbf{x}, \mathbf{y}, \mathbf{z}) \doteq g_i\left(x_i + y_i, x_j, y_j, \mathbf{z}\right) - f_i\left(y_i\right) - t_i(\mathbf{x}), \tag{2}$$

$i, j = 1, 2$, $j \neq i$, where f_i is the firm-specific cost of sourcing y_i internally, and g_i is a gross profit function.[19] In the latter function, firm i's external and internal R&D levels x_i and y_i are added as an

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[16]Here we describe R&D as an output, that is as a service or technology delivered to clients. However it can also be considered as an input, that is as a pecuniary investment level chosen by the lab. Formal examples of the two interpretations are given in Section 4.

[17]The argument $\mathbf{z}$ can represent prices or quantities, indifferently, or refer to more elaborate competitive interactions.

[18]Our common agency model is thus of the *public* kind (Martimort, 2006). This specification differs from most papers that focus on consumer goods markets, where less sophisticated non-compete clauses, hardly verifiable activities, and various antitrust regulations can justify the assumption that a principal can contract exclusively on what it specifically receives from the agent, with no possible connection between payments and the other activities of the agent that benefit a competitor (e.g., Martimort and Stole, 2003).

[19]The form of net profit functions is similar to that considered by Crémer and Riordan (1987) for the modelling of multilateral transactions with bilateral contracts, but with transfer payments that are here contingent on the lab's possible choice of R&D levels.

argument, which formalizes the assumption that external R&D tasks can also be performed inside the firm. However, the respective equilibrium values are the outcome of distinct decision processes that can result in substitutes or complements (y_i^* can be either decreasing or increasing in x_i in Proposition 1, below). The competitor's variables x_j and y_j are arguments of the same function, allowing for technological spillovers through the lab and directly from the competitor. The gross profit also depends on final-market non-cooperative strategies, $\mathbf{z}$.

Timing — There are four stages, as follows:

(i) The two firms simultaneously and non-cooperatively choose a transfer function $t_i(\mathbf{x}) \geq 0$, $i = 1, 2$, that they offer to the lab.

(ii) The lab accepts either both contractual offers simultaneously, or only one, or none, and chooses the firm-specific R&D levels in $\mathbf{x}$ that maximize $v_0(\mathbf{x})$.

At this stage the lab refuses all contracts if they imply lower benefits than the reservation value $\underline{v_0} = 0$, and it takes only one of the two offers if this implies higher benefits than accepting the two contracts.[20] Formally, for any given t_j offered by firm j, the lab accepts firm i's contract offer only if

$$v_0(\mathbf{x}) \geq \sup \left\{ 0, \max_{\mathbf{x}} \{ t_j(\mathbf{x}) - f_0(\mathbf{x}) \} \right\}, \tag{3}$$

for some $\mathbf{x} \geq (0, 0)$, $i, j = 1, 2$, $j \neq i$. As the firms' payments cannot be negative, in equilibrium the participation constraints in (3) are always exactly satisfied.[21] This however does not imply that the equilibrium R&D levels and transfer functions are symmetric, nor that payments are both positive. It can be the case that firm i offers a "null" contract, where $t_i(\mathbf{x}) = 0$, all $\mathbf{x}$, and still receives technology. This occurs for example if limiting inter-firm technological spillovers is prohibitively costly for the lab.

(iii) The firms simultaneously and non-cooperatively choose their own internal R&D level $y_i \geq 0$.

(iv) The firms simultaneously and non-cooperatively choose their final-market strategy $z_i \geq 0$.

Information — The two firms (players) know the strategies available to the other players and the

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[20]As the lab (an agent) can choose to accept only a subset of contracts offered by the two firms (principals), this is a "delegated common agency" model in the terminology introduced by Bernheim and Whinston (1986a).

[21]Should in equilibrium the for-profit lab contract exclusively with, say, firm 1, to deliver $\tilde{\mathbf{x}} \in \arg\max_{\mathbf{x}} \{ t_1(\mathbf{x}) - f_0(\mathbf{x}) \}$, for any $t_2(\tilde{\mathbf{x}}) > (=)0$ it would earn $t_1(\tilde{\mathbf{x}}) - f_0(\tilde{\mathbf{x}}) < (=) t_1(\tilde{\mathbf{x}}) + t_2(\tilde{\mathbf{x}}) - f_0(\tilde{\mathbf{x}})$, a contradiction, so (3) is satisfied. Moreover, should the lab supply $\hat{\mathbf{x}}$ to earn $t_1(\hat{\mathbf{x}}) + t_2(\hat{\mathbf{x}}) - f_0(\hat{\mathbf{x}}) > t_1(\tilde{\mathbf{x}}) - f_0(\tilde{\mathbf{x}})$, then firm 2 would find it profitable to reduce its transfer to $t_2'(\hat{\mathbf{x}}) = t_2(\hat{\mathbf{x}}) - \varphi$, where $\varphi \doteq (t_1(\hat{\mathbf{x}}) + t_2(\hat{\mathbf{x}}) - f_0(\hat{\mathbf{x}})) - (t_1(\tilde{\mathbf{x}}) - f_0(\tilde{\mathbf{x}}))$, for (3) to hold with equality.

related payoffs. This specification does not apply to the lab (an agent), which needs not know the downstream cost and demand conditions. In case of non-deterministic R&D outcomes (see examples 2 and 3 below), the contracts are written *ex ante*, that is before the lab tests technological options, so it has no superior understanding of the stochastic project returns than the client firms (see section 2 on the biopharmaceutical industry context). Information is verifiable by an external enforcer, so that all parties are committed to their contracts.[22]

Equilibrium concept — The results presented in the next section refer to reduced-form expressions of the payoff functions introduced in (2). For any $(\mathbf{x}, \mathbf{y})$, henceforth we assume that there exists a unique final-market Nash equilibrium $\mathbf{z}^*(\mathbf{x}, \mathbf{y})$, so that we may introduce $\hat{g}_i\left(x_i + y_i, x_j, y_j\right) \doteq g_i(x_i + y_i, x_j, y_j, \mathbf{z}^*(\mathbf{x}, \mathbf{y}))$, firm i's reduced-form gross profit.[23] For any $\mathbf{x}$, we also assume that there exists a unique internal R&D stage Nash equilibrium $\mathbf{y}^*(\mathbf{x})$, which allows for the introduction of $\tilde{g}_i\left(\mathbf{x}\right) \doteq \hat{g}_i(x_i + y_i^*(\mathbf{x}), x_j, y_j^*(\mathbf{x})) - f_i\left(y_i^*(\mathbf{x})\right)$, firm i's profit net of internal R&D costs. Finally, for any given $\mathbf{t} \doteq (t_1, t_2)$ denote by $X(\mathbf{t})$ the set of R&D choices that maximize the lab's profits, that is $X(\mathbf{t}) \doteq \arg\max_{\mathbf{x}} v_0(\mathbf{x}(\mathbf{t}))$.

The following definitions are needed before introducing the solution concept: (1) 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 $\tilde{g}_i\left(\mathbf{x}\right) - t_i(\mathbf{x}) \geq \tilde{g}_i\left(\mathbf{x}'\right) - t_i'(\mathbf{x}')$, all t_i'; (2) the transfer function t_i is *truthful* relative to $\tilde{\mathbf{x}}$ if $t_i(\mathbf{x}) \doteq \sup\{0, \tilde{g}_i(\mathbf{x}) - [\tilde{g}_i\left(\tilde{\mathbf{x}}\right) - t_i(\tilde{\mathbf{x}})]\}$.[24]

The solution concept is the truthful subgame-perfect Nash equilibrium (TSPNE). The four-tuple $(\tilde{\mathbf{t}}, \tilde{\mathbf{x}}, \tilde{\mathbf{y}}, \tilde{\mathbf{z}})$ is a TSPNE if, for $i, j = 1, 2, j \neq i$: (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 $\tilde{t}_j$; and (v) $\tilde{t}_i$ is truthful relative to $\tilde{\mathbf{x}}$. It follows that $\tilde{t}_i(\mathbf{x}) = \sup\{0, \tilde{g}_i(\mathbf{x}) - v_i^*\}$, where the constant $v_i^* \doteq \tilde{g}_i(\tilde{\mathbf{x}}) - \tilde{t}_i(\tilde{\mathbf{x}})$ is firm i's equilibrium payoff.

Truthfulness is a standard refinement in delegated common agency games, and two properties in the theoretical literature offer a strong justification for using it (Bernheim and Whinston, 1986b; Laussel and Le Breton, 2001; Martimort, 2007). A first property is that for any set of transfer offers by

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[22]R&D contracts usually include provisions for dispute resolution and point to an external private arbitrager, or to a specific Court, in case of litigation (e.g., Robinson and Stuart, 2007).

[23]Here we follow Amir et al. (2003) by interpreting the reduced-form gross profit function $\hat{g}_i$ as the overall payoff of an infinite-horizon multi-stage game in the product market. Then R&D choices can be seen as long-term decisions, followed by a series of short-term final-market decisions.

[24]When the gross profits $\tilde{g}_i(\mathbf{x})$ exceed $\tilde{v}_i(\tilde{\mathbf{x}})$, the difference between the transfer proposals $t_i(\mathbf{x})$ and $t_i(\tilde{\mathbf{x}})$ is equal to the difference between $\tilde{g}_i(\mathbf{x})$ and $\tilde{g}_i(\tilde{\mathbf{x}})$; otherwise the transfer $t_i(\mathbf{x})$ is set to zero. On its positive part, a truthful contractual offer thus exactly reflects firm i's valuation of $\mathbf{x}$ relative to $\tilde{\mathbf{x}}$.

any of the two firms, there exists a truthful strategy in the other firm's best-response correspondence. A firm can thus restrict itself to truthful strategies. A second property is that all truthful Nash equilibria are coalition-proof. Therefore, the two firms' joint net profits in a TSPNE are not lower than in any other subgame-perfect Nash equilibrium. [25] The proofs of several propositions in Section 4 present the technical challenge[26] of extending fundamental results of this common agency literature to a context where firms not only interact as principals in the intermediate market for external R&D, but also compete in internal technological decisions and in final-market commercial strategies.

Technological assumptions — Each firm's gross profit function is (weakly) increasing in its own R&D levels, as received from the lab or sourced internally (formally $\partial \hat{g}_i / \partial s_i \geq 0$ where $s_i \doteq x_i + y_i$, $i = 1, 2$). However $\hat{g}_i$ can be decreasing, or not, in the rival's arguments, x_j and y_j. In any case a firm's gross profit is (weakly) more impacted by its own R&D, as either purchased from the lab or produced in-house, than by its rival's arguments:

$$\frac{\partial \hat{g}_i}{\partial x_i} \geq \left\| \frac{\partial \hat{g}_i}{\partial x_j} \right\|, \tag{4}$$

$$\| \qquad \vee|$$

$$\frac{\partial \hat{g}_i}{\partial y_i} \geq \left\| \frac{\partial \hat{g}_i}{\partial y_j} \right\|, \tag{5}$$

$i, j = 1, 2$, $j \neq i$. The vertical comparison of the terms on the RHS of the inequality sign in (4) and (5) specifies that the R&D leaks emanating from the lab are more informative than the technological spillovers received from the competitor's internal facilities.[27]

For both firms, returns to R&D can be either non-increasing (that is, $\partial^2 \hat{g}_i / \partial s_i^2 \leq 0$, $i = 1, 2$), or increasing. The sign of all partial cross-derivatives can also be either non-positive (that is, $\partial^2 \hat{g}_i / \partial x_i \partial x_j \leq 0$, $\partial^2 \hat{g}_i / \partial x_i \partial y_j \leq 0$, $\partial^2 \hat{g}_i / \partial y_i \partial x_j \leq 0$, and $\partial^2 \hat{g}_i / \partial y_i \partial y_j \leq 0$, $i, j = 1, 2$, $j \neq i$), or positive. In all cases, the second-order impact of a firm's R&D, either produced in-house or received from the lab, on its own

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[25]A Nash equilibrium is coalition-proof if it is robust to credible threats of deviations by any subset of principals (for a formal definition see Bernheim, Peleg, and Whinston, 1987). With two principals only, a coalition-proof equilibrium is Pareto-efficient among principals (Bernheim and Whinston, 1986b). For a discussion on truthfulness as an equilibrium refinement, see Martimort (2007).

[26]In the appendix, the proofs of Lemmas *A*.1 and *A*.2 establish connections between properties of $\hat{g}_i(\mathbf{x}, \mathbf{y})$ and $\tilde{g}_i(\mathbf{x})$ which are used in combination with theorems by Laussel and Le Breton (2001) and extensions by Billette de Villemeur and Versaevel (2003) to obtain Propositions 2, 3, and 4.

[27]In the words of Lai, Riezman, and Wang (2009), "information leakage is much more severe in the absence of internal controls when R&D is outsourced" (p. 487).

marginal gross profit, is higher than the second-order effect of its competitor's R&D:

$$\left\| \frac{\partial^2 \hat{g}_i}{\partial y_i \partial x_i} \right\| \geq \left\| \frac{\partial^2 \hat{g}_i}{\partial y_i \partial x_j} \right\|, \tag{6}$$

$$\parallel \qquad\qquad \vee\mid$$

$$\left\| \frac{\partial^2 \hat{g}_i}{\partial y_i^2} \right\| \geq \left\| \frac{\partial^2 \hat{g}_i}{\partial y_i \partial y_j} \right\|, \tag{7}$$

$i, j = 1, 2, j \neq i$. Again, the vertical comparison of cross-derivatives in (6) and (7) indicates that each firm's marginal gross profit is more impacted by the technological leakages that emanate from the lab than from its competitor.

These technological assumptions are very mild and encompass many possible specifications of gross profit and cost functions as introduced in the literature (we illustrate with examples of specific algebraic forms in the next section).

Standalone values — The lab can guarantee for itself the value $\underline{v}_0 = 0$ (a normalization). As for the firms, in order to define their outside option, suppose that j has exclusive access to the lab, implying that firm i can rely only on internal resources, $i, j = 1, 2, j \neq i$. Then the contractual relationship between the lab and firm j results in $\mathbf{x}_j^* \in \arg\max_{\mathbf{x}}[\tilde{g}_j(\mathbf{x}) - f_0(\mathbf{x})]$, and firm i can guarantee for itself the standalone value $\underline{v}_i \doteq \tilde{g}_i(\mathbf{x}_j^*)$. Here $\mathbf{x}_j^* \doteq (x_i^*, x_j^*)$, with $x_i^* \geq 0$, so firm i can possibly receive technology, without financial compensation, in spite of firm j's exclusive relationship with the lab. For an equilibrium to exist it must be the case that $v_i^* \geq \underline{v}_i$, for both firms.

4 Technological Conditions and Equilibrium Analysis

In this section, we investigate the circumstances in which technology outsourcing either reduces or stimulates internal R&D levels, before deriving conditions for the lab to appropriate a share of R&D profits, or to exactly break-even to the benefit of the outsourcing firms.

As a first result, we find that in equilibrium each firm's internal R&D level y_i^* can be substitutable or a complementary to the level x_i received from the lab. The sign of the relation between y_i^* and x_i depends on the nature of R&D returns, but not on technological spillovers.

Proposition 1 (external/internal R&D) *The equilibrium level of a firm's internal R&D activity y_i^* is de-*

creasing 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). More formally, for $s_i \doteq x_i + y_i$, and $i = 1, 2$:

$$\frac{dy_i^*}{dx_i} \lessgtr 0 \Leftrightarrow \frac{\partial^2 \hat{g}_i}{\partial s_i^2} \lessgtr 0.^{28} \tag{8}$$

A first message in this proposition is that whether contracted-out R&D reduces or raises internal activity does not depend on inter-firm technological spillovers, because the second-order effect in (8) bears only on each firm i's own argument s_i, not on x_j or y_j, $i, j = 1, 2$, $i \neq j$. This property contrasts with the well-known lesson received from many papers that adopt the analytical framework of d'Aspremont and Jacquemin (1988) in order to focus on *horizontal* technological interactions. In these papers, the strategic substitutability or complementarity of the firms' technological choice variables depends entirely on whether a spillover parameter is low or high, respectively. In our model, the firms also interact *vertically* by competing in their contractual offers to the external unit. This vertical interaction, which is more direct because it occurs through contracting, appears to dominate the horizontal effects for what regards the substitutability/complementarity outcome.

Another message in Proposition 1 is that the relationship between external sourcing and internal R&D activity is formally ambiguous. This ambiguity is structural, in that it depends on the functional form of firms' gross profit. Here contracted-out R&D reduces internal activity if and only if there are decreasing returns to the introduction of cost-reducing or demand-enhancing technology in the firms' operations. This theoretical result is reminiscent of several recent empirical analyses that indicate a context-specific relationship between external and internal R&D sources in the biopharmaceutical industry. In Hagedoorn and Wang (2012) the estimated sign of the marginal effect of internal R&D expenditure on the innovative output is negative, with the marginal returns to internal R&D being possibly lower (higher) than when technology is sourced externally, reflecting a case of substitutability (complementarity). In Ceccagnoli, Higgins, and Palermo (2014), the estimated sign of the partial cross-derivative of an innovation production function with respect to external and internal R&D expenditure is found to depend on a series of factors. These empirical investigations and our formal characterization share the conclusion that external and internal R&D are neither complements not substitutes *per se*, and are rather context related, as captured here by the sign of a second-order effect.

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[28]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 $i, j = 1, 2$, $j \neq i$ (see Appendix A.2).

In what follows we build on Proposition 1 by first considering separately situations of non-increasing returns ($\partial^2 \hat{g}_i / \partial s_i^2 \leq 0$), before discussing the robustness of our results when we shift to non-decreasing returns ($\partial^2 \hat{g}_i / \partial s_i^2 \geq 0$). In the two cases, to characterize the distribution of R&D profits among the intermediate R&D market participants, we need defining as a value function the highest joint profit for the lab together with any subset of firms, that is

$$v(S) \doteq \max_{\mathbf{x}} \left(\sum_{i \in S} \tilde{g}_i(\mathbf{x}) - f_0(\mathbf{x}) \right),$$ (9)

where $S \in \{\varnothing, \{1\}, \{2\}, \{1,2\}\}$.

We assume that $v(\varnothing) = \underline{v}_0 = 0$, which describes the no contract situation, and that $v(\{i\}) \geq \underline{v}_i$, implying that firm i's exclusive control of the lab dominates its standalone value, $i = 1, 2$. Hereafter, for conciseness we denote the maximum industry profit $v(\{1,2\})$ by Λ.

The value function $v(.)$ in (9) is instrumental for the caracterization of equilibrium outcomes in the intermediate market for technology, as it captures the interplay of indirect and direct technological externalities: there are *indirect* technological externalities if the lab's cost f_0 of conducting firm-specific R&D tasks is characterized by economies or diseconomies of scope; there are *direct* externalities if the R&D received or generated by firm i enters in the gross profit function $\hat{g}_j$ of its competitor, $i, j = 1, 2, j \neq i$.[29] Indirect (through the lab) and direct (inter-firm) technological externalities can differ in magnitude and in sign, and an *aggregate measure* of the combination of both categories of externalities is given by the structural parameter

$$\epsilon \doteq \Lambda - v(\{1\}) - v(\{2\}).$$ (10)

If $\epsilon < 0$, that is $v(.)$ is strictly subadditive, the maximization in $\mathbf{x}$ of joint profits generates less value than the sum of individual profits as obtained by each firm when it exclusively controls the lab, a situation where negative externalities dominate. Otherwise $v(.)$ is superadditive, and positive externalities (weakly) dominate.

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[29]In (9), recall that $\tilde{g}_i(\mathbf{x}) \doteq \hat{g}_i(x_i + y_i^*(\mathbf{x}), x_j, y_j^*(\mathbf{x})) - f_i(y_i^*(\mathbf{x}))$, so that firm i's profit does not depend only on x_j, but also on y_j.

■ **Non-increasing returns to R&D**. In this section we assume that

$$\frac{\partial^2 \hat{g}_i}{\partial s_i^2} \leq 0, \tag{11}$$

$i = 1, 2$. Simple sufficient conditions on the primitives of the model can now be derived for the joint R&D benefits in equilibrium to be either fully appropriated by the two firms, or partly retained by the lab. These conditions bear on the sign of indirect and direct R&D externalities, hence on the lab's costs $f_0(\mathbf{x})$ and the firms' reduced-form gross profit functions $\hat{g}_i(x_i + y_i, x_j, y_j)$, respectively.

Non-negative R&D externalities. Suppose, as a first case, that indirect and direct R&D externalities are non-negative. Formally, for $i, j = 1, 2, j \neq i$,

$$\frac{\partial^2 f_0}{\partial x_i \partial x_j} \leq 0, \tag{12}$$

$$\frac{\partial \hat{g}_i}{\partial x_j} \geq 0, \quad \frac{\partial \hat{g}_i}{\partial y_j} \geq 0. \tag{13}$$

Proposition 2 (non-negative R&D externalities) *Conditions* (12-13) *imply that $\epsilon \geq 0$. There exists a continuum of firm equilibrium payoffs $(v_1^*, v_2^*) \geq (\underline{v}_1, \underline{v}_2)$ that verify*

$$v_1^* + v_2^* = \Lambda, \tag{14}$$

and the lab exactly breaks even, that is

$$v_0^* = 0. \tag{15}$$

In (12) the non-positive sign of the cross-derivatives of f_0 in the dimensions of $\mathbf{x}$ describes economies of scope in the production of R&D inside the external lab. Selecting a higher x_i, as demanded by firm i, makes it less costly for the lab to satisfy firm j.[30] This condition is consistent with empirical investigations that evidence the presence of economies of scope in drug discovery (Henderson and Cockburn, 1996) and clinical trials (Cockburn and Henderson, 2001).

For an interpretation of the conditions in (13), recall from the structure of each firm's gross profit function in (2) that R&D decisions generate not only technological (or knowledge) spillovers (x_j and y_j are arguments of g_i, $j \neq i$) but also a product-market rivalry effect (firm j's external and internal

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[30]As Pisano (2006) puts it, "knowledge and capabilities accumulated in the pursuit of one therapeutic area can often be leveraged to others" (p. 101).

R&D impacts firm i's strategy z_i, $j \neq i$). As the two non-negative derivatives in (13) relate to the reduced-form $\hat{g}_i$ of the gross profit expression, they capture situations where technological spillovers dominate the negative business stealing effect. This specification points to situations of substantial spillovers, as observed by Henderson (1994) and Henderson and Cockburn (1996) between pharmaceutical firms. It is also consistent with Bloom et al. (2013) where significant technological spillovers, and business stealing effects, are found in the pharma industry, together with strategic complementarity in R&D (*e.g.*, the latter property applies in Example 4 below, case $\beta \geq 1/2$).

Non-negative indirect and direct externalities reflect circumstances of weak technological rivalry among the two firms, both in their contractual offers to the lab and in their internal operations, implying a limited ability of the external lab to appropriate R&D benefits. This theoretical characterization is consistent with the empirical observation that the average profitability of biotech units is persistently low. Proposition 2 actually establishes that the two firms appropriate all industry profits, and the lab exactly breaks even.[31] Therefore:

Corollary 1 *When conditions (12-13) hold, incentives to invest in the external unit are delinked from the value generated to the exclusive benefit of downstream sponsors.*

The following example illustrates Proposition 2 with specific cost and demand functional forms borrowed from the R&D literature.

Example 1 □ *Symeonidis (2003) constructs a duopoly model with product R&D. For each firm inverse demand is $p_i(q_i, q_j) = S\left(1 - \frac{2q_i}{u_i^2} - \frac{\sigma}{u_i}\frac{q_j}{u_j}\right)$, $i,j = 1,2$, $j \neq i$, where S is the number of identical consumers, $\sigma \in (0,2)$ captures horizontal product differentiation, and u_i measures firm i's product quality, which depends on R&D. Specifically, let $u_i = \varepsilon(s_i)^{1/4} + \varepsilon\beta(s_j)^{1/4}$, where $\varepsilon > 0$ is an inverse cost measure, $\beta \in [0,1]$ is an inter-firm technological parameter, $s_i \doteq x_i + y_i$ and $s_j \doteq x_j + y_j$.[32] If $x_1 = x_2 = 0$ we have the original model, otherwise external R&D contributes to innovation. We set $S = \sigma = \varepsilon = 1$, $\beta = 1/2$, and production costs to zero for simplicity, and solve for the firms' market stage Cournot-Nash equilibrium 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 $\frac{dy_i^*}{dx_i} < 0$ (contracted-out R&D reduces internal activity). 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*

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[31]In Appendix A.4 we show that there always exists $v_i^* \geq \underline{v}_i$, $i = 1,2$, such that the pair (v_1^*, v_2^*) verifies (14). The continuum of equilibrium payoffs is thus well defined.

[32]This functional form is adapted from Motta (1992).

that (13) *is satisfied.*[33] *Then any additive cost function for the external lab, e.g.* $f_0(\mathbf{x}) = x_1 + x_2$, *satisfies* (12), *hence Proposition 2 applies, and the client firms fully appropriate R&D benefits.* □

Negative R&D externalities. Suppose now that indirect and direct R&D externalities are negative, that is for $i, j = 1, 2, j \neq i$,

$$\frac{\partial^2 f_0}{\partial x_i \partial x_j} > 0, \tag{16}$$

$$\frac{\partial \hat{g}_i}{\partial x_j} \leq 0, \quad \frac{\partial \hat{g}_i}{\partial y_j} \leq 0. \tag{17}$$

Proposition 3 (negative R&D externalities) *Conditions* (16-17) *imply that* $\epsilon < 0$. *There is a unique pair of firm equilibrium payoffs* (v_1^*, v_2^*), *which are*

$$v_i^* = v(\{i\}) - |\epsilon| \geq \underline{v}_i, \tag{18}$$

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

$$v_0^* = |\epsilon| > 0. \tag{19}$$

The condition on f_0 in (16) formalizes a case of congestion, or diseconomies of scale, in the production of R&D by the external lab. Supplying more R&D to a given firm makes it more costly to serve the other firm. The conditions on $\hat{g}_i$ in (17) describe circumstances in which more of firm j's R&D, as sourced externally or produced internally, weakly reduces firm i's reduced-form gross profit, all other things remaining equal. Together, these formal conditions relate to real-world circumstances that strongly differ from the ones captured by conditions $(12 - 13)$. Unlike the empirical evidence mentioned in the previous section on early-stage discovery activities that involve biotech entities, diseconomies of scope (Macher and Boerner, 2006) and nonexistent technological spillovers (Danzon et al. 2005; Macher and Boerner, 2006) have been found in later-stage development activities, notably in phase 2 and phase 3 clinical trials, which involve CROs. The formal conditions in (16) and (17) clearly point to these development activities.

In such cases of negative indirect and direct externalities, the client firms compete for the control of the lab's operations in the intermediate R&D market, and are also penalized by the in-house activity of their competitor. These circumstances are favorable to the lab. Proposition 3 establishes

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[33]The expressions of derivatives are omitted for space limitation. They are available from the authors on request.

that negative externalities fully drive the distribution of R&D benefits. Unlike the payoff in the previous section, the lab here appropriates a positive share of industry profits, in direct proportion to $-\epsilon$ which is positive. Each firm's payoff is equal to $v(\{i\})$, $i = 1, 2$, as would be earned by controlling the lab exclusively, truncated by $|\epsilon|$. The latter payoff can be shown to be greater that the standalone value $\underline{v}_i$.[34] The theoretical outcome that the external unit extracts a positive share is consistent with the observation that CROs involved in clinical trials, unlike biotech units, on average earn superior average financial returns.

Differentiability — Although stated in terms of cross-derivatives, the condition in (16) can be rewritten in discrete form as $f_0(\mathbf{x} \wedge \mathbf{x}') + f_0(\mathbf{x} \vee \mathbf{x}') - f_0(\mathbf{x}) - f_0(\mathbf{x}') \geq 0$, all $\mathbf{x}, \mathbf{x}' \in X$, with a strict inequality whenever $\mathbf{x}$ and $\mathbf{x}'$ cannot be compared with respect to $\geq$ (strict supermodularity). The condition in (17) can also be rewritten as $\hat{g}_i\left(x_i + y_i, x_j, y_j\right) \geq \hat{g}_i(x_i + y_i, x'_j, y'_j)$ for all $(x'_j, y'_j) \geq (x_j, y_j)$. In the whole paper differentiability is adopted for notational convenience, but is not required, as illustrated by the next example.[35]

Example 2 □ *Assume that* $\mathbf{x}, \mathbf{y} \in \{0, 1\}^2$, *so the decision to invest in a cost-reducing program implies a lump-sum expenditure. The lab's R&D costs are* $f_0(\mathbf{x}) = 0$ *if* $x_1 = x_2 = 0$, $f_0(\mathbf{x}) = 1$ *if* $x_1 + x_2 = 1$, *and* $f_0(\mathbf{x}) = +\infty$ *otherwise, so that the discrete form of condition* (16) *is satisfied. Here anti-complementarities imply that the lab serves at most one firm profitably* ($x_1 = x_2 = 1$ *is excluded*).[36] *Firm i's internal R&D costs are* $f_i(y_i) = \gamma y_i$, *with* $\gamma \geq 1$ *capturing a relative inefficiency vis-à-vis the lab. The unit cost of production is a positive constant* $c_i(x_i + y_i)$, *with* $c_i(0) = c_H$ *and* $0 \leq c_i(1) = c_i(2) = c_L < c_H$. *The two firms sell a homogeneous good, with total demand* $q = \sup\{0, a - p\}$, *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* $\hat{g}_i\left(x_i + y_i, x_j, y_j\right) = 0$ *otherwise, so the discrete form of condition* (17) *is also satisfied. We assume that internal R&D is worth undertaking, that is* $\gamma/\pi < 1$. *To compute equilibrium payoffs, we consider the following two cases: (1) If the lab is inactive* ($x_1 = x_2 = 0$), *there exists a unique Nash equilibrium in mixed strategies* (α_i^*, α_j^*) *of internal R&D investments, verifying*

$$\alpha_j^* \times (-\gamma) + \left(1 - \alpha_j^*\right) \times (\pi - \gamma) = \alpha_j^* \times 0 + \left(1 - \alpha_j^*\right) \times 0, \tag{20}$$

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[34]See Appendix A.4). From (10) the payoff to the lab can be rewritten as firm i's marginal contribution to industry profit, that is $v_i^* = \Lambda - v(\{j\})$, $i, j = 1, 2$, $j \neq i$.

[35]In Appendix A.4 the proofs of Propositions 2 and 3 are written for any f_0 which is either weakly submodular or strictly supermodular, respectively.

[36]The cost specification in this example, with f_0 strictly supermodular, is borrowed from Laussel and Le Breton (2001).

i, j = 1, 2, *j* ≠ *i. By symmetry*[37]

$$\alpha_i^* = \alpha_j^* = 1 - \frac{\gamma}{\pi},$$

which leads to the payoff $v_i(\alpha_1^*, \alpha_2^*) = \underline{v}_i = 0$, $i = 1, 2$.[38] *So the firms are willing to transact with the lab.* (2) *When the lab is active, from the assumption on* f_0 *only one firm is served* ($x_i = 1 > x_j = 0$), *and no firm invests in internal R&D since* $\hat{g}_i(1 + 1, 0, y_j) - f_i(1) < \hat{g}_i(1 + 0, 0, y_j) - f_i(0)$, *all* y_j, *and* $\hat{g}_j(0 + 1, 1, y_i) - f_j(1) < \hat{g}_j(0 + 0, 1, y_i) - f_j(0)$, *all* y_i. *Therefore, industry value is* $v(\{1, 2\}) = v(\{1\}) = v(\{2\})$, *so that* $v_0^* = v(\{1, 2\}) = \pi - 1$, *and* $v_i^* = v(\{1, 2\}) - v(\{j\}) = 0$, *from Proposition 3. Firms' interests are so antagonistic in this example as to make the lab fully appropriate industry value.* □

Uncertainty — Although the examples above describe a deterministic environment, the structural conditions in Propositions 2 and 3 also capture circumstances in which R&D outcomes are uncertain for all parties. To see that, consider the same specifications as in Example 2, but with the lab and the firms being successful in R&D with probability ρ. Here it can be useful for a firm to invest simultaneously with the lab to increase the probability of success. The unit cost of production $c(x_i + y_i)$ is now $c(0) = c_H$ with certainty, $c_i(1) = c_L$ with probability ρ and $c_i(1) = c_H$ with probability $1 - \rho$, and $c_i(2) = c_L$ with probability $1 - (1 - \rho)^2$ and $c_i(2) = c_H$ with probability $(1 - \rho)^2$. Here the distribution of (un)favorable events is common knowledge ex ante, and the true state is discovered only through the realization of R&D tasks. Condition (16) remains unchanged, and although the process is now uncertain, condition (17) also remains valid in expectation, as the choice of firm j to attempt to innovate always reduces firm i's expected profit. Thus Proposition 3 still holds. We assume as above that R&D is worth undertaking, even internally, that is $\gamma/(\rho\pi) < 1$. Provided that the probability of success ρ remains sufficiently close to 1 so that $1 - \rho < \gamma/(\rho\pi)$, again a firm will not engage in R&D if its rival receives technology from the lab or sources it internally, and we can directly generalise the baseline example: (1) If the lab is inactive ($x_1 = x_2 = 0$), there exists a unique symmetric Nash equilibrium in mixed strategies

$$\alpha_i^*(\rho) = \alpha_j^*(\rho) = \frac{1}{\rho}\left(1 - \frac{\gamma}{\rho\pi}\right),$$

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[37]Given that in this example firms are assumed to be symmetric, we leave aside the two asymmetric equilibria in pure strategies ($y_1^* = 0, y_2^* = 1$) and ($y_1^* = 1, y_2^* = 0$).

[38]In this example, when firm i does not participate in the R&D market, its rival j receives technology from the relatively more efficient lab (so $x_j^* = 1$), exclusively so ($x_i^* = 0$), and finds it profitable not to operate internally ($y_j^* = 0$). Then in this Bertrand context firm i maximizes profits by not investing in internal R&D, and its standalone value is $\underline{v}_i = \hat{g}_i(0 + y_i^*, 1, 0) - f_i(y_i^*) = \hat{g}_i(0 + 0, 1, 0) - f_i(0) = 0$, $i, j = 1, 2, j \neq i$.

for a payoff which again is the same as the standalone value $\underline{v}_i(\rho) = 0$, $i = 1, 2$, so the firms have an incentive to transact with the lab. (2) When the lab is active, again from the assumption on f_0 only one firm is served ($x_i = 1 > x_j = 0$), and limited uncertainty does not modify the outcome that no firm invests internally since, rewritting payoff functions in expected terms, $E_\rho\left[\hat{g}_i(1+1, 0, y_j)\right] - f_i(1) < E_\rho\left[\hat{g}_i(1+0, 0, y_j)\right] - f_i(0)$, all y_j, and $E_\rho\left[\hat{g}_j(0+1, 1, y_i)\right] - f_j(1) < E_\rho\left[\hat{g}_j(0+0, 1, y_i)\right] - f_j(0)$, all y_i. The payoff of the firm that does not receive external R&D is nil, so that $v(\{1, 2\}) = v(\{1\}) = v(\{2\})$. Then $v_0^* = v(\{1, 2\})$, and $v_i^* = v(\{1, 2\}) - v(\{j\}) = 0$, $i, j = 1, 2, j \neq i$, from Proposition 3.

With these specifications, the lab is granted the (positive) expected industry profit, here equal to $\rho\pi - 1$, while the firm that benefits from the lab's output exactly breaks even only in expectation, and its rival earns its standalone value for sure.

In the next example, we show that our results also apply to the polar situation with highly uncertain R&D. We obtain that, when the competitor or its external contractor might fail with a high probability, it can be a dominant strategy for the firms to engage in R&D as well.

Example 3 □ *We consider the specifications of Example* 2 *with the extension to uncertain R&D considered above, and focus on the case of rare successful outcomes. R&D can be profitable, that is $\gamma/(\rho\pi) < 1$, although the probability of success ρ is sufficiently close to 0 for $\gamma/(\rho\pi) < (1-\rho)^2$ to hold. In this case, the likelihood that the competitor and the lab succeed in R&D is so low as to make the probability of simultaneous success negligible. Then everything happens as if, when deciding to engage or not in R&D, each firm were focusing on its own probability of success only, abstracting from the other players' actions. Investing in internal R&D is a dominant strategy: (1) If the lab is inactive ($x_1 = x_2 = 0$), the firms' expected payoff is $(1-\rho)\rho\pi - \gamma$, which is slightly higher than the standalone level $\underline{v}_i(\rho) = (1-\rho)^2\rho\pi - \gamma$, $i = 1, 2$. (2) When the lab is active, again the form of f_0 implies that only one firm is served ($x_i = 1 > x_j = 0$). Still the distinctive feature here, in comparison to the previous example, is that both firms choose to invest internally as well: $E_\rho\left[\hat{g}_i(1+1, 0, y_j)\right] - f_i(1) > E_\rho\left[\hat{g}_i(1+0, 0, y_j)\right] - f_i(0)$, all y_j, and $E_\rho\left[\hat{g}_j(0+1, 1, y_i)\right] - f_j(1) > E_\rho\left[\hat{g}_j(0+0, 1, y_i)\right] - f_j(0)$, all y_i. Thus $v(\{i\}) = \left[1 - (1-\rho)^2\right](1-\rho)\pi - \gamma - 1$ (i.e., π is earned by firm i when the latter player and the lab do not both fail while firm j fails) and the industry expected value is now $v(\{1, 2\}) = (3 - 2\rho)(1-\rho)\rho\pi - 2\gamma - 1$ (the sum of firm i's expected gross payoff $\left[1 - (1-\rho)^2\right](1-\rho)\pi$ and of firm j's gross payoff $(1-\rho)^2\rho\pi$ net of total R&D costs). Therefore, from Proposition 3 we have $v_0^* = (1-\rho)\rho\pi - 1 > 0$, and $v_i^* = v(\{1, 2\}) - v(\{j\}) = (1-\rho)^2\rho\pi - \gamma$, which is positive but remains equal to the firms' standalone level, $i, j = 1, 2, j \neq i$. By competing for the lab's resources, the firms earn*

less than if the lab is simply not available.□

There is more in Examples 2 and 3 than an illustration of the applicability of the theoretical propositions to specific algebraic forms. Only in the latter example, where the probability of success of R&D operations is assumed to be low, both the lab and its sponsor engage in R&D efforts. This outcome is consistent with the empirical evidence (Guedj, 2005) that projects with a low probability of success are more often conducted through a contractual alliance between a large firm and a smaller biotech company (as in Example 3) than conducted entirely within the same entity (as in Example 2). The comparison of examples 2 and 3 thus rationalizes the general observation that the reduction in drug R&D productivity over the last decades – which is formally captured here by a lower probability of success – has coincided with increasingly frequent situations where large pharma firms and smaller external biotech units contribute jointly to research and development (Pisano, 2006; Rydzewski, 2008; Scannell et al., 2012). This is a sufficiently high level of uncertainty, in our theoretical framework, that triggers an investment by all industry participants.

Another interesting equilibrium property illustrated by examples 2 and 3 is that client firms (principals), whose payments to the lab are truthful, are shielded from the uncertainty that is specific to external R&D operations. The lab (agent), however, bears the risk inherent to its technological activities. When the equilibrium payoff to the lab, in expectation, is exactly zero (Proposition 2), then an unfavorable draw necessarily yields a negative net return. To summarize:

Corollary 2 *When R&D externalities are non-negative ($\epsilon \geq 0$), efficient projects at the industry level are vulnerable to unfavorable events that affect the external unit.*

In order to avoid the abandonment of projects that are characterized by a high degree of technological uncertainty, but also contribute positively to total industry profits, one can think of some safeguarding measures that were not considered in our model specifications – including public intervention. Such measures, in light of our results and their connections to the empirical evidence, appear less relevant for clinical trials (development) than for early-stage research activities (discovery) characterized by significant economies of scope and technological spillovers. The financial backup of a partner university, as commonly observed in the early stages of startups since emergence of biotechnology in the late 1970s, can thus be interpreted in retrospect as a relevant attempt to insure promising spin-offs from unfavorable events. This interpretation however does not apply to direct

cash subsidies, since in our model they would only lower the lab's break-even point, to the benefit of client firms.

We now consider cases with increasing returns to R&D.

■ **Non-decreasing returns to R&D**. In this section, for $i = 1, 2$, we assume that

$$\frac{\partial^2 \hat{g}_i}{\partial s_i^2} \geq 0, \tag{21}$$

where $s_i \doteq x_i + y_i$. We identify simple conditions for Propositions 2 and 3 to remain valid.

Proposition 4 *Suppose that returns to R&D are non-decreasing, as in* (21). *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* $\frac{dy_j^*}{dx_i} > -1$.

The interplay of contracted-out and internal R&D levels is central to our results.

From Proposition 1, we know that increasing R&D returns imply that $\frac{dy_j^*}{dx_j} \geq 0$, which is sufficient to obtain that $\frac{d\tilde{g}_i}{dx_j}$ has the same sign as $\frac{\partial \hat{g}_i}{\partial x_j}$ and $\frac{\partial \hat{g}_i}{\partial y_j}$ (see Lemma $A.1$ in Appendix A.3). As for the sign of $\frac{d\tilde{g}_i}{dx_i}$, it depends also on $\frac{dy_j^*}{dx_i}$. There are two cases. If x_j and x_i are complementary inside firm i's gross payoff function, so that $\frac{\partial^2 \hat{g}_j}{\partial x_j \partial x_i} \geq 0$, then y_j^* is monotone increasing in x_i, that is $\frac{dy_j^*}{dx_i} \geq 0$. It follows that $\frac{d\tilde{g}_i}{dx_i}$ has the same sign as $\frac{\partial \hat{g}_i}{\partial x_j}$ and $\frac{\partial \hat{g}_i}{\partial y_j}$ (see Lemma $A.2$), and Propositions 2 and 3 remain valid with non-decreasing returns as well. When x_i and x_j are substitutable, in that $\frac{\partial^2 \hat{g}_j}{\partial x_j \partial x_i} < 0$, then y_j^* decreases in x_i, that is $\frac{dy_j^*}{dx_i} < 0$. Here more R&D purchased from the lab reduces the other firm's internal R&D level. In the most extreme circumstances, the latter effect could possibly result in $\frac{d\tilde{g}_i}{dx_i}$ being negative when $\frac{\partial \hat{g}_i}{\partial x_j}$ and $\frac{\partial \hat{g}_i}{\partial y_j}$ are both positive. The latter property however does not occur when the substitution effect is limited, more specifically when $\frac{dy_j^*}{dx_i} > -1$.

The next example illustrates all cases predicted by Proposition 4. It shows that while external and internal R&D tasks are complementary (a consequence of non-decreasing returns to R&D from Proposition 1), the client firms fully appropriate industry profit (as in Proposition 2) or concede to the lab a positive share of it (as in Proposition 3).

Example 4 □ *The cost of the external lab is* $f_0(\mathbf{x}) = (x_1 + x_2)^2 - \delta x_1 x_2 / 2$, *with* $\delta \geq 0$, *and the internal R&D cost is* $f_i(y_i) = \kappa + y_i^2$, $i = 1, 2$, *with* $\kappa > 0$. *The marginal cost of operations is* $c_i(\mathbf{x}) = (c - s_i - \beta s_j)$,

with $c > 0$, with an inter-firm spillover parameter $\beta \in [0,1]$ as in d'Aspremont and Jacquemin (1988), and where $s_i = x_i + y_i$ can be interpreted as the sum of R (that is, x_i) and D (y_i) as in Vonortas (1994). The final-market inverse demand is $p(\mathbf{q}) = a - q_i - q_j$, with $a > c$. Non-cooperative profit maximization in quantities leads to $q_i^*(\mathbf{x}, \mathbf{y}) = [(a - c) + s_i(2 - \beta) + s_j(2\beta - 1)]/3$. We have $\partial^2 \hat{g}_i / \partial s_i^2 = 2(2 - \beta)^2/9 > 0$, so condition (21) is satisfied for all parameter values (increasing R&D returns). Then, whether Proposition 2 or 3 applies depends on δ and β: (i) if $\delta \geq 1 (< 1)$ then condition (12) (resp. condition (16)) holds; (ii) if $\beta \geq 1/2 (< 1/2)$ then condition (13) (resp. condition (17)) holds, directly from $\partial \hat{g}_i / \partial x_j = \partial \hat{g}_i / \partial y_j = (2/3)(2\beta - 1) q_i^*(\mathbf{x}, \mathbf{y})$. Moreover, $\partial^2 \hat{g}_i / \partial x_j \partial x_i = (2/9)(2 - \beta)(2\beta - 1) \geq 0$ only if $\beta \geq 1/2$, and we have $dy_j^*/dx_i = 3(2\beta - 1)(\beta - 2)/[(\beta^2 - \beta + 7)(\beta^2 - 3\beta - 1)] > -1$ for $\beta < 1/2$. Therefore, in this example the non-negative R&D externalities case of Proposition 2 applies if $\beta \geq 1/2$ and $\delta \geq 1$, and the negative externalities case of Proposition 3 applies if $\beta < 1/2$ and $\delta < 1$. $\square$

An important lesson of Propositions 2 and 3 is that the interplay of indirect (through the lab) and direct (inter-firm) technological externalities drives the additivity status of the value function v in (9), which in the end determines the distibution of industry profits. This characterization applies in all situations where the two types of externalities have the same sign, as formalized by the easy-to-use benchmark conditions (12-13) and (16-17). It applies also in "mixed" cases where indirect externalities are negative, while direct externalities are not, or *vice versa*.

For an illustration, consider again the previous example by setting $\delta = \beta = 0$, but by assuming that the firms rely exclusivey on the exernal lab ($y_1 = y_2 = 0$), so that their gross reduced-form profits are similar to the ones considered in Ho (2009).[39] Here we have non-negative indirect but negative direct externalities ($\partial^2 f_0 / \partial x_1 \partial x_2 = 0$ and $\partial \hat{g}_i / \partial x_j < 0$ for all positive final-market quantities). Simple computations lead to $v(\{1\}) = v(\{2\}) = (a - c)^2/5$, and $\Lambda = (a - c)^2/4$, a case of strict subadditivity, implying from (18) that equilibrium payoffs are $v_1^* = v_2^* = v_0^*/3 = (a - c)^2/20$.

5   Incentives for More Integration

The distribution of industry profits can be modified either by a coordination of contract offers by the two firms, or by a shift to a more vertically integrated structure that unifies the lab with one of the two

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[39]In Ho (2009) the magnitude of the cost reduction, as obtained from the external lab, is specified to be exogenous (whereas it is chosen by the for-profit lab in the present case), and the final market inverse demand function involves a slope parameter b (which is set equal to 1 here).

firms, or both. In this section we investigate the link between the sign of technological externalities and incentives for more integration of some kind in the intermediate R&D market.[40]

Suppose that the owners of the three entities can participate in the equity market in order to possibly depart from the initial outsourcing equilibrium characterized in the previous section. We assume that (i) initially, each entity is owned by distinct sets of individuals (no one can simultaneously be a seller and a buyer); (ii) when the lab and only one firm integrate vertically, the unified entity can agree to supply R&D to the other firm by bargaining with it over the sharing of industry profits; and (iii) transaction costs are nil.

Consider first the situation in which the lab and the two firms all participate in some form of integration on the intermediate R&D market. This occurs if the lab acquires the two firms and controls them as subsidiaries, or if the two firms share the ownership of the lab and control it as a joint venture, with choices of internal R&D and final-market strategies remaining non cooperative (no collusion). In these two cases there is no gain in joint profits to be earned vis-à-vis equilibrium payoffs of the common agency structure. This is because the truthfulness of the firms' equilibrium payment strategies implies that the lab is offered two transfer schedules which exactly reflect the respective shapes of the firms' gross profit functions (that is, $\tilde{g}_i\left(\mathbf{x}\right) \doteq \hat{g}_i(x_i + y_i^*(\mathbf{x}), x_j, y_j^*(\mathbf{x})) - f_i\left(y_i^*(\mathbf{x})\right)$, $i = 1, 2$). The lab thereby internalizes both direct and indirect externalities, and thus is incentivized to supply R&D outputs that maximize the joint profits of all participants.[41] It follows that the net residual share of joint profits accruing to each buyer of another firm's equity cannot improve on the amount of net profits received in the common agency equilibrium. Forward integration (i.e., the two users become subsidiaries of the lab) would imply the payment of v_i^* by the lab to the firms' owners. Backward integration (i.e., the lab becomes a joint venture) would require the total payment of v_0^* by the two firms for the ownership of the upstream assets. The equality $v_0^* + v_1^* + v_2^* = \Lambda$ holds in all cases, unless further assumptions are introduced (e.g., cost or demand parameters become a function of the governance structure). More formally:

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[40]Our choice to characterize first the equilibrium profit distribution in the decentralized common agency setting, before investigating incentives to integrate in the intermediate market for new biotechnology, reflects industry practice (Folta, 1998; Danzon and Grabowski, 2012).

[41]To compare, in Spulber (2013) joint profits are not maximized when an upstream inventor charges a two-part royalty (an up-front lump-sum royalty and a royalty per unit of output produced with its cost-reducing innovation) to downstream firms, which sell differentiated products in the final market. A positive per-unit royalty is chosen as it results in an implicit collusion mechanism from which the inventor benefits through the lump-sum royalty. The per-unit royalty implies double marginalization, and hence suboptimal profits at the industry level.

Proposition 5 *In the initial outsourcing situation, the firms' non-cooperative equilibrium transfer payments and the lab's individual profit-maximizing R&D outputs $\tilde{\mathbf{x}}$ result in a maximum industry profit: $\tilde{\mathbf{x}} \in \arg\max_{\mathbf{x} \in X} (\tilde{g}_1(\mathbf{x}) + \tilde{g}_2(\mathbf{x}) - f_0(\mathbf{x}))$. Therefore, unless the firms coordinate internal R&D operations ($\mathbf{y}$) or collude in final-market commercial decisions ($\mathbf{z}$), there is no incentive for the lab to acquire the two firms and control them as subsidiaries, nor for the firms to share the ownership of the lab and control it as a joint venture.*

In other words, the integration of all market participants is profitable only if the firms neutralize downstream strategic interactions by coordinating internal R&D activities or/and final-market strategies.

It remains to investigate all alternative forms of integration that can allow the respective owners of the lab, or of the two firms, to privately appropriate a larger share of the industry maximum Λ than in the decentralized outsourcing initial situation. Toward an equilibrium industry structure in the equity market, we consider the following discrete set of possible arrangements: the horizontal integration of firms 1 and 2 for the joint procurement of external R&D (internal R&D and final-market choices remaining non cooperative), the vertical integration of the lab with firm 1, or with firm 2. We consider in turn the situations in which the value function v (in (9)) is superadditive ($\epsilon \geq 0$, as in Proposition 2), then strictly subadditive ($\epsilon < 0$, as in Proposition 3), depending on the interplay of indirect (through the lab) and direct (inter-firm) technological externalities. The two cases are illustrated respectively by Figures 1 and 2, which represent the space of possible partitions of the maximum industry profit Λ as a 2-simplex, with full appropriation by the lab (i.e., $v_0 = \Lambda$) at the top vertex, and by either of the two firms at the bottom vertices. More generally, the payoffs to the lab and each of the two firms are proportional to the distance of the allocation point to the edge opposite to their respective vertex.

Non-negative R&D externalities   When indirect and direct R&D externalities are both non-negative, or in "mixed" situations with positive and negative externalities where the former dominate, so that v is superadditive ($\epsilon \geq 0$), from Proposition 2 the lab only breaks even in equilibrium of the common agency structure, that is $v_0^* = 0$, and the two firms thus appropriate the maximized industry profit, $v_1^* + v_2^* = \Lambda$ (where $v_i^* \geq \underline{v}_i$, $k = 1, 2$).

As there exists a continuum of firm equilibrium payoffs, the exact distribution (v_1^*, v_2^*) can only reflect circumstances outside of the initial model specifications. Hereafter we formalize such circum-

stances by the bargaining powers (ϕ_1, ϕ_2) in $[0,1]^2$, with $\phi_1 + \phi_2 = 1$. They verify

$$v_k^* = \underline{v}_k + \phi_k \left(\Lambda - \underline{v} \right), \tag{22}$$

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

$$\phi_k = \frac{v_k^* - \underline{v}_k}{\Lambda - \underline{v}}. \tag{23}$$

Although with non-negative externalities joint R&D procurement cannot increase the firms' joint profit, a larger individual share can be earned by a firm if it deviates unilaterally from the outsourcing equilibrium to acquire the lab. By exclusively controlling of the lab, the vertically integrated entity $\{0, i\}$ benefits from a stronger bargaining position. In case of disagreement its payoff becomes $v\left(\{i\}\right) \geq \underline{v}_i$, while its rival j's payoff remains at $\underline{v}_j$, the standalone value. The bargaining process, in case of vertical integration, thus determines a payoff to the unified entity equal to

$$v_{0+i}^{\{0,i\}} = v\left(\{i\}\right) + \phi_i \left(\Lambda - v\left(\{i\}\right) - \underline{v}_j \right) \geq v_i^*, \tag{24}$$

and a payoff to the outsider equal to

$$v_j^{\{0,i\}} = \underline{v}_j + \phi_j \left(\Lambda - v\left(\{i\}\right) - \underline{v}_j \right) \leq v_j^*, \tag{25}$$

with the weights (ϕ_i, ϕ_j) as defined in (23), $i, j = 1, 2, j \neq i$.[42]

As they face two competing alternatives, the lab's owners can choose the firm to integrate with.[43] By selling out to firm i, they earn $v_0^{\{0,i\}} = v_{0+i}^{\{0,i\}} - v_i^{\{0,i\}}$, the difference beween the payoff to the unified entity and the acquirers' residual claim. The two firms' respective owners thus compete in the equity market, and their willingness to pay is the difference between the value they generate by acquiring

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[42]There is a strict inequality sign in (25) if $v\left(\{i\}\right) > \underline{v}_i$, because firm j has the same disagreement value $\underline{v}_j$ as in the initial outsourcing equilibrium. In that case, a strict inequality in (24) would follow from $v_{0+i}^{\{0,i\}} + v_j^{\{0,i\}} = v_i^* + v_j^* = \Lambda$, implying that $v_{0+i}^{\{0,i\}} - v_i^* = v_j^* - v_j^{\{0,i\}} > 0$.

[43]For completeness, if the exclusive control of the lab strictly dominates the standalone option only for firm i, so that $v\left(\{i\}\right) > \underline{v}_i$ and $v\left(\{j\}\right) = \underline{v}_j$, then $v_{0+j}^{\{0,j\}} = v_j^*$. As there is no incentive for the latter firm j to integrate vertically, in that case firm i acquires the lab (it pays $\varepsilon > v_0^* = v_0^{\{1,2\}} = 0$ with ε arbitrarily small), and the equilibrium structure is $\{0, i\}$, with payoffs as in (24-25). If there is no gain to the exclusive control of the lab for both firms, so that $v\left(\{i\}\right) = \underline{v}_i$ as well, then no firm is interested in acquiring the lab, and the initial outsourcing equilibrium structure prevails.

the lab and the value they earn should the lab integrate with the other firm. In comparison to the initial equilibrium situation, the firm that does not integrate, say firm j, is forced to concede what the other firm appropriates by acquiring the lab. Firm i's willingness to pay, as an acquirer, is thus the sum of what it appropriates, and what the other would have appropriated, that is

$$v_{0+i}^{\{0,i\}} - v_i^{\{0,j\}} = \phi_j \left(v\left(\{i\}\right) - \underline{v}_i \right) + \phi_i \left(v\left(\{j\}\right) - \underline{v}_j \right) \geq 0, \tag{26}$$

$i, j = 1, 2, j \neq i$. Therefore, although firms are asymmetric, and thus appropriate different amounts by acquiring the lab, the willingness to pay is the same across the two firms. Then competition in the equity market results in the integration of the lab with any of the two firms, indifferently.
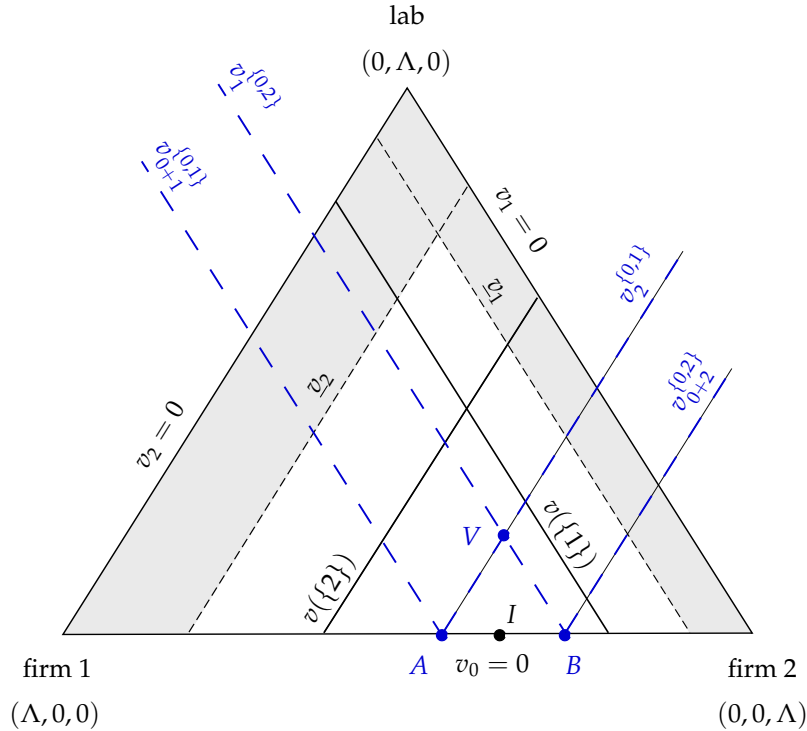

Figure 1: v is superadditive ($\epsilon \geq 0$), so the loci for $v\left(\{1\}\right)$ and $v\left(\{2\}\right)$ intersect inside the simplex. In the initial equilibrium (point I), the firms fully appropriate industry profits ($v_1^* + v_2^* = \Lambda$), so the lab exactly breaks even ($v_0^* = 0$). Should a firm integrate the lab at no cost, it would appropriate more industry profits (point A for firm 1, or B for firm 2). However, competition in the equity market lowers firms' payoffs to $v_i^{\{0,j\}}$, for $i, j = 1, 2, j \neq i$, and in the lab to appropriate positive profits, that is $v_0^{\{0,1\}} = v_0^{\{0,2\}} > 0$ (point V).

In the equilibrium industry structure, the winning firm i's owners have bidden their willingness to pay so they receive only $v_i^{\{0,j\}} \leq v_i^*$, and the rival j's owners, by contracting out for R&D with the integrated entity $\{0,i\}$, earn only $v_j^{\{0,i\}} \leq v_j^*$. The lab's owners earn a payoff equal to the common

maximum bid, which from (23) and (26) is equal to

$$v_0^{\{0,1\}} = v_0^{\{0,2\}} = \frac{v(\{1\}) - \underline{v}_1}{\Lambda - \underline{v}}\left(v_2^* - \underline{v}_2\right) + \frac{v(\{2\}) - \underline{v}_2}{\Lambda - \underline{v}}\left(v_1^* - \underline{v}_1\right) > v_0^* = 0, \qquad (27)$$

with the *strict* inequality replaced by an equality sign only in the degenerate case where $v(\{i\}) = \underline{v}_i$ for the two firms $i = 1, 2$.[44] The lab's owners, whose payoffs are nil in the initial R&D market equilibrium, eventually extract a positive share of industry profits in the equity market (point V in Figure 1). Eventually, this outcome points to long-term incentives to invest in early-stage research activities (discovery), although the short-term profitability is nil (see Proposition 2).

Negative R&D externalities   When indirect and direct R&D externalities are both negative, or in "mixed" situations with positive and negative externalities where the latter dominate, so that v is strictly subadditive ($\epsilon < 0$), from Proposition 3 the equilibrium payoffs in the initial outsourcing situation are $v_0^* = |\epsilon| > 0$, and $v_i^* = v(\{i\}) - |\epsilon| \geq \underline{v}_i$, $i = 1, 2$, so that $v_1^* + v_2^* < \Lambda$. As an alternative to the initial outsourcing situation, the firms can opt for an horizontal arrangement in order to procure jointly external R&D. In that case they behave cooperatively as a unique principal on the intermediate market for technology, and fully appropriate the maximum industry profit, with the lab breaking even exactly (point H in Figure 2 below).[45] We thus have $v_0^{\{1,2\}} = 0$ and $v_1^{\{1,2\}} + v_2^{\{1,2\}} = \Lambda$ (here the superscript $\{1, 2\}$ refers to the industry structure with firms 1 and 2 procuring jointly).

The initial outsourcing equilibrium payoffs determine the firms' disagreement point (v_1^*, v_2^*) when they bargain over the agent's payoff $v_0^* = \Lambda - v_1^* - v_2^*$. The outcome payoffs $\left(v_1^{\{1,2\}}, v_2^{\{1,2\}}\right)$ verify

$$v_k^{\{1,2\}} = v_k^* + \omega_k\left(\Lambda - v_1^* - v_2^*\right), \qquad (28)$$

where $k = 1, 2$, implying that bargaining powers (ω_1, ω_2) in $[0, 1]^2$, with $\omega_1 + \omega_2 = 1$, are

$$\omega_k = \frac{v_k^{\{1,2\}} - v_k^*}{\Lambda - v_1^* - v_2^*}. \qquad (29)$$

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[44]Otherwise, even if $v_i^* = \underline{v}_i$ for one of the two firms (say $i = 1$), the inequality in (27) remains strict (as necessarily $v_2^* - \underline{v}_2 = \Lambda - \underline{v} - (v_1^* - \underline{v}_1) > 0$).

[45]A horizontal arrangement here relates to the intermediate market for technology, as opposed to the final market for products, where the firms are assumed to remain competitors. This situation is similar to the cases observed by Majewski (2004) where firms engaged in a technology alliance jointly choose to outsource their R&D to a third party in order to split costs.
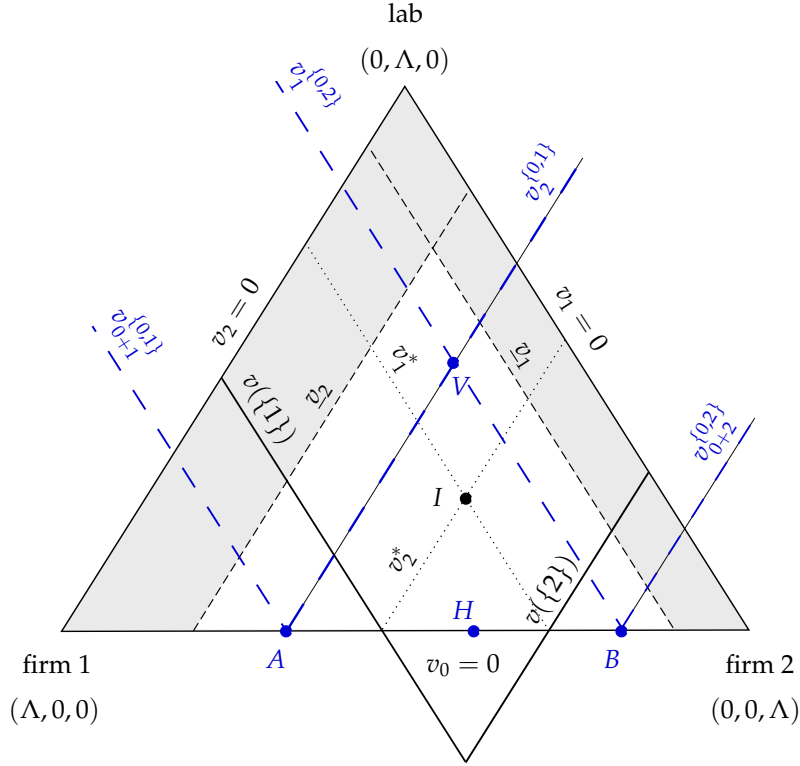
Figure 2: v is strictly subadditive ($\epsilon < 0$), so the loci for $v(\{1\})$ and $v(\{2\})$ intersect outside the simplex. In the initial R&D equilibrium (point I) the firms earn $v_i^* = v(\{i\}) - |\epsilon|$, $i = 1, 2$, and the lab earns $v_0^* > 0$. By agreeing horizontally to coordinate R&D outsourcing, the firms fully reappropriate industry profits (point H). Should a firm integrate vertically with the lab, at no cost, it would increase profits (point A for firm 1, or B for firm 2). The bidding contest to acquire the lab leads both firms to earn $v_i^{0,j}$, $i, j = 1, 2$, $j \neq i$ (point V) in the equilibrium industry structure.

From Proposition 3 we know that $v_0^* = \Lambda - v_1^* - v_2^* > 0$, implying that in (28) we have $v_k^{\{1,2\}} \geq v_k^*$ for $k = 1, 2$, with a *strict* inequality sign for at least one firm, implying that at least one firm earns a positive gain by shifting to the horizontal arrangement. Moreover, the definition of ϵ in (10) together with $v_i^* = v(\{i\}) - |\epsilon|$ in (18) imply that $v_j^* = \Lambda - v(\{i\})$, so that $v_j^{\{1,2\}} \geq v_j^*$ and $v_j^{\{1,2\}} = \Lambda - v_i^{\{1,2\}}$ lead to $v_i^{\{1,2\}} \leq v(\{i\})$, $i, j = 1, 2$, $j \neq i$, again with a *strict* inequality sign for at least one firm. It follows that

$$v(\{k\}) - |\epsilon| \leq v_k^{\{1,2\}} \leq v(\{k\}), \tag{30}$$

where $k = 1, 2$, with at least one *strict* inequality sign. In (30) the first inequality states that any situation resulting in lower individual payoffs than in the initial equilibrium is rejected. The second inequality indicates that each firm's payoff in the horizontal arrangement is bounded from above by $v(\{i\})$, the value generated when it acquires the external lab without contracting with its rival.

While the two firms' joint profit is maximized in the horizontal arrangement, each firm has an

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incentive to depart unilaterally from $\{1,2\}$ by acquiring the lab, for a *strictly*[46] higher disagreement payoff $v\left(\{i\}\right) > v_i^*$ accruing to the integrated entity $\{0,i\}$, and a (weakly) lower disagreement payoff $\underline{v}_j \leq v_j^*$ to the other firm. By controlling the lab and benefitting exclusively from its technology, in case of disagreement the integrated entity can guarantee for itself the upper bound of the horizontal arrangement payoff in (30), while the outsider earns only its standalone value. The bargaining process, with vertical integration, implies a payoff to the unified entity equal to

$$v_{0+i}^{\{0,i\}} = v\left(\{i\}\right) + \omega_i \left(\Lambda - v\left(\{i\}\right) - \underline{v}_j\right) > v_i^{\{1,2\}}, \tag{31}$$

and a payoff to the outsider equal to

$$v_j^{\{0,i\}} = \underline{v}_j + \omega_j \left(\Lambda - v\left(\{i\}\right) - \underline{v}_j\right) < v_j^{\{1,2\}}, \tag{32}$$

$i,j = 1,2$, $j \neq i$.[47] The lab's owners, as in the non-negative externalities situation of the previous section, can thus make the two firms compete in the equity market by soliciting bids in order to reappropriate a positive share of industry profits. Provided that no restriction is introduced that limits payment offers, again the firms have the same willingness to pay for the lab, that is

$$v_{0+i}^{\{0,i\}} - v_i^{\{0,j\}} = \omega_j \left(v\left(\{i\}\right) - \underline{v}_i\right) + \omega_i \left(v\left(\{j\}\right) - \underline{v}_j\right) > 0, \tag{33}$$

$i,j = 1,2$, $j \neq i$, and any of them becomes the acquirer with equiprobability. The payoffs structure already obtained in the non-negative externalities case thus prevails, with each firm's owners earning exactly their outside value, $v_1^{\{0,2\}} < v_1^{\{1,2\}}$ and $v_2^{\{0,1\}} < v_2^{\{1,2\}}$, in any of the two possible equilibrium industry structures.

However, with negative externalities it is not *a priori* established that the lab's owners are better-off post integration than in the initial outsourcing equilibrium. Inserting the expression of the firms' respective bargaining powers in (33), and reorganizing terms (see Appendix $A.6$), we find that

$$v_0^{\{0,1\}} = v_0^{\{0,2\}} = \frac{v\left(\{1\}\right) - \underline{v}_1}{|\epsilon|} \left(v_2^{\{1,2\}} - v_2^*\right) + \frac{v\left(\{2\}\right) - \underline{v}_2}{|\epsilon|} \left(v_1^{\{1,2\}} - v_1^*\right) \geq v_0^* = |\epsilon|. \tag{34}$$

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[46]In this negative externalities situation ($\epsilon \doteq \Lambda - v\left(\{i\}\right) - v\left(\{j\}\right) < 0$) we have $v\left(\{i\}\right) > \Lambda - v\left(\{j\}\right) = v_i^*$.

[47]The strict inequality sign in (32) is a consequence of $v\left(\{i\}\right) > v_i^* \geq \underline{v}_i$, and possibly of firm j's strictly lower disagreement value $\underline{v}_j < v_j^*$ (this differs from the non-negative externalities case in (25)). Then the strict inequality in (31) follows from $v_i^{\{1,2\}} + v_j^{\{1,2\}} = v_{0+i}^{\{0,i\}} + v_j^{\{0,i\}} = \Lambda$, which leads to $v_{0+i}^{\{0,i\}} - v_i^{\{1,2\}} = v_j^{\{1,2\}} - v_j^{\{0,i\}} > 0$.

This establishes that, with negative externalities, the value that can be extracted by the owners of the external unit, by selling out to any of the two – possibly asymmetric – client firms (from *I* to *V* in Figure 2), is only *weakly* superior to the positive profits earned in the initial outsourcing equilibrium.

To summarize:

Proposition 6 *Suppose that the exclusive control of the lab strictly dominates a firm's standalone option* $(v(\{i\}) > \underline{v}_i, i = 1, 2)$:

(a) If the firms can commit not to integrate the lab they fully appropriate industry profits: (i) with non-negative R&D externalities $(\epsilon \geq 0)$, *the firms remain independent and the initial outsourcing equilibrium prevails; (ii) with negative R&D externalities* $(\epsilon < 0)$, *the firms engage in the horizontal arrangement* $\{1, 2\}$ *to coordinate external technology sourcing; (iii) in both cases the firms fully appropriate industry value* Λ, *and the lab's financial return is nil.*

(b) Otherwise, independently of the sign of R&D externalities, one of the two firms acquires the lab with the same probability $1/2$, *and competition in the equity market drives firms' payoffs down to* $v_1^{\{0,2\}}$ *and* $v_2^{\{0,1\}}$, *with* $v_1^{\{0,2\}} + v_2^{\{0,1\}} < \Lambda$, *to the benefit of the lab's owners who extract* $\Lambda - v_1^{\{0,2\}} - v_2^{\{0,1\}} \geq v_0^*$.

The latter results point to several simple empirical implications that connect technological characteristics to the type of acquisitions that modify the structure of the market for R&D. In part (a) of Proposition 6 we focus on cases where the firms, for some exogenous reasons (e.g., a regulation, or a strategic orientation), rule out the possibility to acquire the lab. When technological externalities are non-negative $(\epsilon \geq 0)$, because multi-client R&D operations benefit from economies of scope, or inter-firm knowledge spillovers are significant, then the industry structure is more likely to remain decentralized with no downstream coordination. In the alternative where externalities are negative $(\epsilon < 0)$, the firms are more likely to coordinate technology sourcing from the same external lab. This second category of situations is reminicent of Majewski (2004), where evidence is found that "when collaborative agreements involve firms that compete in downstream markets, they tend to outsource their collaborative R&D to a third party" (p. 2).

Moreover, in part (b) of Proposition 6 we learn that competition among client firms is more profitable to the lab's owners in the equity market than in the R&D market, independently of the identity of the acquirer. Competition is tougher in the equity market, as only one firm can acquire the lab,

whereas in the R&D market firms can partially reconcile their antagonism through finely tuned contract offers. As discussed from an empirical perspective by Higgins and Rodriguez (2006), the firms overbid for the external unit, and the acquirer succumbs to the winner's curse. More recently, Pisano (2015) also reflected on whether "pharmaceutical companies [are] paying more for R&D by acquiring companies than by carrying out the R&D themselves". According to our result, pharmaceutical companies pay more for R&D by acquiring an external unit in the market for equity than by contracting in the market for technology. This theoretical outcome points to the exit payoff as a long-term financial incentive that can motivate the foundation of a new R&D company in the first place. However, we have learned above that incentives to sell out the equity are weaker in the case of negative externalities, since profits are already positive in the initial R&D market equilibrium, and they can only be weakly augmented in the equity market (comparison of (27) with (34)).

Corollary 3 *From the viewpoint of the lab's 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).*

Financial constraints — Finally, note that Proposition 6 is derived under the assumption that bids are unrestricted. However, in real-world business circumstances a financial constraint might be introduced that limits firms' ability to compete for the control of an external entity. In the theoretical context of the model, the effect of such a constraint can be investigated by assuming that the payoff to the lab's owners, in case of vertical integration, cannot be so high as to imply a lower payoff to the acquiring firm than in the initial outsourcing equilibrium. Formally, the two firms' respective financial constraints are thus

$$v_i^* \leq v_i^{\{0,i\}} = \Lambda - v_j^{\{0,i\}} - v_0^{\{0,i\}}, \tag{35}$$

$i, j = 1, 2, j \neq i.$

In principle such a constraint makes it more difficult for a firm to acquire the lab when the latter makes positive profits than when it exactly breaks even. It also helps identifying the profile of the most agressive bidder. With non-negative R&D externalities ($\epsilon \geq 0$), as $\Lambda - v_i^* = v_j^*$ from Proposition 2, firm i's constraint in (35) becomes $v_0^{\{0,i\}} \leq v_j^* - v_j^{\{0,i\}}$. In other words, firm i's maximum bid, when it acquires the lab, must not exceed what firm j has lost, as an outsider, because of the change in bargaining positions vis-à-vis the outsourcing situation. By using (22) and (25), firm i's financial constraint can thus be rewritten $v_0^{\{0,i\}} \leq \phi_j \left(v \left(\{i\} \right) - \underline{v}_i \right)$, $i, j = 1, 2, j \neq i$. The lab's owners face two

competing bids, and select the highest, say the one of firm i if $\phi_j \left(v \left(\{i\} \right) - \underline{v}_i \right) \geq \phi_i \left(v \left(\{j\} \right) - \underline{v}_j \right)$ which, by using (23), is equivalent to

$$\frac{v_i^* - \underline{v}_i}{v \left(\{i\} \right) - \underline{v}_i} \leq \frac{v_j^* - \underline{v}_j}{v \left(\{j\} \right) - \underline{v}_j}. \tag{36}$$

The comparison in (36) predicts that the acquirer is the firm whose net equilibrium payoff in the initial outsourcing situation (that is $v_i^* - \underline{v}_i$), relatively to the net profit that the integrated entity can guarantee for itself ($v \left(\{i\} \right) - \underline{v}_i$), is lower.

With negative R&D externalities ($\epsilon < 0$), the same reasoning starting from (35) leads to the following condition for firm i to be the one that acquires the lab:

$$\frac{v_i^{\{1,2\}} - \underline{v}_i}{v(\{i\}) - |\epsilon| - \underline{v}_i} \leq \frac{v_j^{\{1,2\}} - \underline{v}_j}{v(\{j\}) - |\epsilon| - \underline{v}_j}. \tag{37}$$

Here the acquirer is the firm whose relative gain in the horizontal arrangement (that is $v_i^{\{1,2\}} - \underline{v}_i$), relatively to the initial equilibrium net payoff ($v_i^* - \underline{v}_i = v(\{i\}) - |\epsilon| - \underline{v}_i$), is lower. The theoretical prediction of conditions (36 - 37) is compatible with the empirical evidence that the most active firms in the equity market are not the ones with the highest profit prospects nor the deepest pockets. In Higgins and Rodriguez (2006), the firms experiencing a deterioration of their research pipeline are found to be more likely to engage in the acquisition of a biotech entity. In Danzon, Epstein, and Nicholson (2007), the financially strong firms appear to be less likely to engage in acquisitions.

6 Conclusion

Our analysis offers a rationalization of the general proposition that, depending on specific circumstances, outsourced and in-house R&D operations might prove substitutable or complementary, as substantiated by the most recent empirical evidence in the biopharmaceutical context (Hagedoorn and Wang, 2012; Ceccagnoli, Higgins, and Palermo, 2014). In our formal setting, each firm's internal equilibrium effort can be decreasing or increasing with the external unit's activity. The direction of change is formally ambiguous because it depends on profit functions being characterized by decreasing or increasing returns to R&D. In the latter case which is commonly associated with those process

or product innovations with most potential, the choice by big pharma firms to contract with an external unit should *not* be interpreted as a form of disinvestment. It corresponds to circumstances where external R&D complements, rather than substitutes for, internal operations.

We derive formal conditions for the industry profit to be either fully absorbed downstream, or partly appropriated by the external unit. These conditions, which match remarkably well the empirical evidence, only depend on the sign and magnitude of indirect (through the unit) and direct (inter-firm) technological externalities. The case of negative externalities points to clinical trial activities (development), where diseconomies of scope and limited or nonexistent inter-firm spillovers were identified in empirical studies of reference (Danzon et al. 2005; Macher and Boerner, 2006). We also identify situations where for any probability of success the external unit appropriates all of the profits, in a "buyer's market" where client firms behave as principals and are no less informed than the external unit. However, the model shows that there can be circumstances where positive externalities soften inter-firm competition in contract offers, so that the external unit can only exactly break even in equilibrium. It follows that incentives to invest upstream are delinked from the value of the knowledge generated by the external unit to its downstream sponsors, and the ability of investors to realize a non-negative net return is highly vulnerable to unfavorable events. The formal conditions that characterize such circumstances capture cases of economies of scope in biotech projects, and of significant technological spillovers among pharma firms, such as evidenced in drug discovery (research) activities by several important empirical papers (Henderson and Cockburn, 1996; Cockburn and Henderson, 2001; Bloom et al., 2013).

But still, longer-term positive incentives to invest can be identified – including in cases of early-stage research – that relate to the equity market, where several possible industry configurations emerge in our model, in accordance with the large variety of restructuring activities observed in the biopharmaceutical context (Danzon and Grabowski, 2012). Depending on the sign of the technological externalities, the initial decentralized outsourcing scenario might prevail, or firms might engage in a horizontal agreement for the coordination of technology outsourcing. When the firms cannot commit not to acquire the external unit, vertical integration occurs and a bidding war leads the acquirer to overpay its target, although the premium is only weakly positive in the case of negative externalities that are characteristic of later-stage development tasks. This result gives theoretical support to the observation that real-world biotech owners, more than CRO founders involved in

clinical trials, are likely to extract – or reappropriate – more industry value by selling their assets to big pharma firms than by running R&D projects.

Overall, our formal analysis offers a new rationale for the low average profitability of the science-based businesses of biotech observed since the emergence of genetic engineering in the 1970s (Pisano, 2006, 2010). In light of our results, and their connection with empirical observations, we believe that limited financial returns should not be seen as evidence of disappointing technological progress, but can be interpreted as a confirmation that economies of scope and knowledge spillovers have been significant in the biotechnology domain. Indeed, in such circumstances, which in our theoretical framework do not generalize to the market for development services, our propositions suggest that the decision by competing firms to outsource early-stage research activities to a common external unit results in most value – possibly very substantial – to be appropriated by the large downstream sponsors.

The delinkage of upstream investment incentives from total industry value, and the vulnerability of investors' net returns to negative shocks, together theorize the abandonment of projects precisely in those early-stage areas that can generate critical advances toward new treatments or preventives. An important consequence is that, although the internalization of indirect (through the lab) and direct (inter-firm) positive externalities is a source of efficiency gains, and the long-term perspective of selling out assets induces incentives to start a biotech unit, research outsourcing may not always qualify as a relevant pathway to address the declining productivity in innovation issue that has characterized the industry over several decades.

We close by observing that it would be interesting to extend our analysis in a number of ways. The firms' contractual offers, which in our model connect each firm's payment to the external lab's R&D operations, could be enriched by additional contracting elements, such as a share of revenues, or an outcome of the regulatory process (e.g., approval by the FDA). Another possible extension would be to depart from the symmetric information context by assuming that a firm and the external unit know better the risk of the specific project in which they are involved than the other firm. We could also depart from the (realistic) assumption that big pharma companies behave as principals, in order to compare our results with a theoretical benchmark where the external R&D unit, instead of responding to its sponsors' payment schemes, makes contractual offers to the firms. This is left for further research.

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A   Appendix

We first develop the derivatives $\frac{dy_j^*}{dx_j}$ and $\frac{dy_i^*}{dx_j}$, which are needed to prove Propositions 1 to 4 afterwards.

A.1   Derivation of $\frac{dy_j^*}{dx_j}$ and $\frac{dy_i^*}{dx_j}$

As the arguments x_i and y_i enter additively into g_i (hence $\hat{g}_i$), we have

$$\frac{\partial \hat{g}_i \left(x_i + y_i^*, x_j, y_j^* \right)}{\partial x_i} - \frac{\partial f_i \left(y_i^* \right)}{\partial y_i} = 0, \tag{38}$$

and similarly

$$\frac{\partial \hat{g}_j \left(x_j + y_j^*, x_i, y_i^* \right)}{\partial x_j} - \frac{\partial f_j \left(y_j^* \right)}{\partial y_j} = 0, \tag{39}$$

where the Nash strategies $y_i^* \doteq y_i^* (x_i, x_j)$ and $y_j^* \doteq y_j^* (x_i, x_j)$ result from the two firms' non-cooperative profit-maximization in their respective internal R&D levels, for $i, j = 1, 2, j \neq i$.

Differentiating (38) and (39) w.r.t. x_j, and using again $s_i \doteq x_i + y_i$ in $\hat{g}_i$, and $s_j \doteq x_j + y_j$ in $\hat{g}_j$, we obtain the system of equations

$$\begin{pmatrix} \frac{\partial^2 \hat{g}_i}{\partial x_i \partial y_j} & \frac{\partial^2 \hat{g}_i}{\partial x_i^2} - \frac{\partial^2 f_i}{\partial y_i^2} \\ \frac{\partial^2 \hat{g}_j}{\partial x_j^2} - \frac{\partial^2 f_j}{\partial y_j^2} & \frac{\partial^2 \hat{g}_j}{\partial x_j \partial y_i} \end{pmatrix} \begin{pmatrix} \frac{dy_j^*}{dx_j} \\ \frac{dy_i^*}{dx_j} \end{pmatrix} = \begin{pmatrix} -\frac{\partial^2 \hat{g}_i}{\partial x_i \partial x_j} \\ -\frac{\partial^2 \hat{g}_j}{\partial x_j^2} \end{pmatrix},$$

where $\hat{g}_i \doteq \hat{g}_i \left(x_i + y_i^*, x_j, y_j^* \right)$, $\hat{g}_j \doteq \hat{g}_j \left(x_j + y_j^*, x_i, y_i^* \right)$, $f_i \doteq f_i (y_i^*)$, and $f_j \doteq f_j(y_j^*)$, for clarity.

This yields the solution

$$\begin{pmatrix} \frac{dy_j^*}{dx_j} \\ \frac{dy_i^*}{dx_j} \end{pmatrix} = \frac{1}{\Delta} \begin{pmatrix} -\frac{\partial^2 \hat{g}_j}{\partial x_j \partial y_i} & \frac{\partial^2 \hat{g}_i}{\partial x_i^2} - \frac{\partial^2 f_i}{\partial y_i^2} \\ \frac{\partial^2 \hat{g}_j}{\partial x_j^2} - \frac{\partial^2 f_j}{\partial y_j^2} & -\frac{\partial^2 \hat{g}_i}{\partial x_i \partial y_j} \end{pmatrix} \begin{pmatrix} -\frac{\partial^2 \hat{g}_i}{\partial x_i \partial x_j} \\ -\frac{\partial^2 \hat{g}_j}{\partial x_j^2} \end{pmatrix} \tag{40}$$

where

$$\Delta \doteq \left(\frac{\partial^2 \hat{g}_i}{\partial x_i^2} - \frac{\partial^2 f_i}{\partial y_i^2} \right) \left(\frac{\partial^2 \hat{g}_j}{\partial x_j^2} - \frac{\partial^2 f_j}{\partial y_j^2} \right) - \frac{\partial^2 \hat{g}_i}{\partial x_i \partial y_j} \frac{\partial^2 \hat{g}_j}{\partial x_j \partial y_i}. \tag{41}$$

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We thus have

$$\frac{dy_j^*}{dx_j} = \frac{1}{\Delta}\left[\frac{\partial^2 \hat{g}_j}{\partial x_j \partial y_i}\frac{\partial^2 \hat{g}_i}{\partial x_i \partial x_j} - \left(\frac{\partial^2 \hat{g}_i}{\partial x_i^2} - \frac{\partial^2 f_i}{\partial y_i^2}\right)\frac{\partial^2 \hat{g}_j}{\partial x_j^2}\right], \tag{42}$$

$$\frac{dy_i^*}{dx_j} = \frac{1}{\Delta}\left[\frac{\partial^2 \hat{g}_i}{\partial x_i \partial y_j}\frac{\partial^2 \hat{g}_j}{\partial x_j^2} - \left(\frac{\partial^2 \hat{g}_j}{\partial x_j^2} - \frac{\partial^2 f_j}{\partial y_j^2}\right)\frac{\partial^2 \hat{g}_i}{\partial x_i \partial x_j}\right]. \tag{43}$$

We know that $\frac{\partial^2 f_i(y_i^*)}{\partial y_i^2} \geq 0$ (by assumption) and $\frac{\partial^2 \hat{g}_i}{\partial x_i^2} - \frac{\partial^2 f_i}{\partial y_i^2} < 0$ (second-order condition), which holds also for firm j. As $\frac{\partial^2 \hat{g}_i}{\partial x_i \partial y_j}$ and $\frac{\partial^2 \hat{g}_j}{\partial x_j \partial y_i}$ have the same sign (by assumption), $\left\|\frac{\partial^2 \hat{g}_i}{\partial x_i^2}\right\| \geq \left\|\frac{\partial^2 \hat{g}_i}{\partial x_i \partial y_j}\right\|$ and $\left\|\frac{\partial^2 \hat{g}_j}{\partial x_j^2}\right\| \geq \left\|\frac{\partial^2 \hat{g}_j}{\partial x_j \partial y_i}\right\|$ (see (7)), we obtain from (41) that $\Delta \geq 0$.[48]

Moreover, we know also from Henriques (1990) that the reaction functions in the internal R&D space (y_i, y_j) cross "correctly", so that the Nash equilibrium (y_i^*, y_j^*) is stable, only if

$$\left|\frac{\partial^2 \left[\hat{g}_i\left(x_i + y_i, x_j, y_j\right) - f_i\left(y_i\right)\right]}{\partial y_i^2} \middle/ \frac{\partial^2 \left[\hat{g}_i\left(x_i + y_i, x_j, y_j\right) - f_i\left(y_i\right)\right]}{\partial y_i \partial y_j}\right| < 1, \tag{44}$$

for $i, j = 1, 2$, $j \neq i$.

Again, the argument $s_i \doteq x_i + y_i$ in $\hat{g}_i$, together with f_i being a function of y_i only, imply that $\frac{\partial^2 \left[\hat{g}_i\left(x_i + y_i, x_j, y_j\right) - f_i\left(y_i\right)\right]}{\partial y_i \partial y_j} = \frac{\partial^2 \hat{g}_i\left(x_i + y_i, x_j, y_j\right)}{\partial y_i \partial y_j} = \frac{\partial^2 \hat{g}_i\left(x_i + y_i, x_j, y_j\right)}{\partial x_i \partial y_j}$, so that (44) becomes $\left|\left(\frac{\partial^2 \hat{g}_i}{\partial x_i^2} - \frac{\partial^2 f_i}{\partial y_i^2}\right) \middle/ \frac{\partial^2 \hat{g}_i}{\partial x_i \partial y_j}\right| < 1$. The latter inequality, together with $\frac{\partial^2 \hat{g}_i}{\partial x_i^2} - \frac{\partial^2 f_i}{\partial y_i^2} < 0$ for $i = 1, 2$ (second-order condition) and $\frac{\partial^2 \hat{g}_i}{\partial x_i \partial y_j}\frac{\partial^2 \hat{g}_j}{\partial x_j \partial y_i} \geq 0$ for $i, j = 1, 2$, $j \neq i$ (partial cross-derivatives, for both firms, have the same sign by assumption) imply from (41) that Δ is nonzero at (y_i^*, y_j^*), and the derivatives in (42) and (43) are well defined.

Suppose now that $\frac{\partial^2 \hat{g}_i}{\partial x_i^2}$ is nonzero for $i = 1, 2$ (the case $\frac{\partial^2 \hat{g}_i}{\partial x_i^2} = 0$ is considered below in the proof of Proposition 1). Then, a careful reorganization of terms in the expression of $\frac{dy_j^*}{dx_j}$ in (42) leads to

$$\frac{dy_j^*}{dx_j} = \frac{-\frac{\partial^2 \hat{g}_j}{\partial x_j^2}}{\frac{\partial^2 \hat{g}_j}{\partial x_j^2} - \frac{\partial^2 f_j}{\partial y_j^2}}\left[1 - \frac{\frac{\partial^2 \hat{g}_j}{\partial x_j \partial y_i}}{-\frac{\partial^2 \hat{g}_j}{\partial x_j^2}}\frac{N_{jj}}{\Delta}\right], \tag{45}$$

where $N_{jj} \doteq \frac{\partial^2 \hat{g}_i}{\partial x_i \partial y_j}\frac{\partial^2 \hat{g}_j}{\partial x_j^2} - \left(\frac{\partial^2 \hat{g}_j}{\partial x_j^2} - \frac{\partial^2 f_j}{\partial y_j^2}\right)\frac{\partial^2 \hat{g}_i}{\partial x_i \partial x_j}$.

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[48]From the expression in (2), the argument $s_i \doteq x_i + y_i$ of the gross profit function g_i, hence also of the reduced-form $\hat{g}_i$, implies that inequalities (6 - 7) can be rewritten by substituting the derivatives with respect to x_i for the ones with respect to y_i. Thus $\partial^2 \hat{g}_i / \partial y_i \partial x_i = \partial^2 \hat{g}_i / \partial x_i^2$, $\partial^2 \hat{g}_i / \partial y_i \partial x_j = \partial^2 \hat{g}_i / \partial x_i \partial x_j$, and $\partial^2 \hat{g}_i / \partial y_i \partial y_j = \partial^2 \hat{g}_i / \partial x_i \partial y_j$, for $i, j = 1, 2$, $i \neq j$. We make use of these substitutions throughout the appendix.

Similarly, a reorganization of terms in the expression of $\frac{dy_i^*}{dx_j}$ in (43) leads to

$$\frac{dy_i^*}{dx_j} = \frac{-\frac{\partial^2 \hat{g}_i}{\partial x_i \partial x_j}}{\frac{\partial^2 \hat{g}_i}{\partial x_i^2} - \frac{\partial^2 f_i}{\partial y_i^2}} \left[1 - \frac{\frac{\partial^2 \hat{g}_i}{\partial x_i \partial y_j}}{-\frac{\partial^2 \hat{g}_i}{\partial x_i \partial x_j}} \frac{N_{ij}}{\Delta} \right], \tag{46}$$

where $N_{ij} \doteq \frac{\partial^2 \hat{g}_j}{\partial x_j \partial y_i} \frac{\partial^2 \hat{g}_i}{\partial x_i \partial x_j} - \left(\frac{\partial^2 \hat{g}_i}{\partial x_i^2} - \frac{\partial^2 f_i}{\partial y_i^2} \right) \frac{\partial^2 \hat{g}_j}{\partial x_j^2}$.

Both expressions in (45) and (46) are well defined because the denominators of their respective first terms are nonzero by assumption (second-order condition for a unique $\mathbf{y}^*(\mathbf{x})$).

A.2 Proof of Proposition 1.

We want to establish that $\frac{dy_i^*}{dx_i} < 0 \Leftrightarrow \frac{\partial^2 \hat{g}_i}{\partial s_i^2} < 0$, where $s_i \doteq x_i + y_i$, and with $\hat{g}_i \doteq \hat{g}_i \left(x_i + y_i^*, x_j, y_j^* \right)$, $\hat{g}_j \doteq \hat{g}_j \left(x_j + y_j^*, x_i, y_i^* \right)$, $f_i \doteq f_i (y_i^*)$, and $f_j \doteq f_j(y_j^*)$, $i, j = 1, 2$, $j \neq i$, throughout this section for clarity. There are three cases:

Case 1: $\frac{\partial^2 \hat{g}_i}{\partial s_i^2} = 0$. Recalling from $s_i \doteq x_i + y_i$ in $\hat{g}_i$ that $\frac{\partial^2 \hat{g}_i}{\partial y_i \partial x_i} = \frac{\partial^2 \hat{g}_i}{\partial x_i^2}$ and $\frac{\partial^2 \hat{g}_i}{\partial y_i \partial x_j} = \frac{\partial^2 \hat{g}_i}{\partial x_i \partial x_j}$, from (6) we have $\left\| \frac{\partial^2 \hat{g}_i}{\partial y_i \partial x_i} \right\| = \left\| \frac{\partial^2 \hat{g}_i}{\partial x_i^2} \right\| = 0 \geq \left\| \frac{\partial^2 \hat{g}_i}{\partial y_i \partial x_j} \right\| = \left\| \frac{\partial^2 \hat{g}_i}{\partial x_i \partial x_j} \right\|$, implying that $\frac{\partial^2 \hat{g}_i}{\partial x_i \partial x_j} = 0$. Then, by inserting $\frac{\partial^2 \hat{g}_i}{\partial x_i^2} = 0$ and $\frac{\partial^2 \hat{g}_i}{\partial x_i \partial x_j} = 0$ into (42) and (43) we find

$$\frac{dy_j^*}{dx_j} = \frac{dy_i^*}{dx_j} = 0. \tag{47}$$

Case 2: $\frac{\partial^2 \hat{g}_i}{\partial s_i^2} < 0$. (i) Here $\frac{\partial^2 f_i(y_i^*)}{\partial y_i^2} \geq 0$ implies that $\frac{\partial^2 \hat{g}_i}{\partial x_i^2} - \frac{\partial^2 f_i}{\partial y_i^2} \leq \frac{\partial^2 \hat{g}_i}{\partial x_i^2} < 0$, while $\left\| \frac{\partial^2 \hat{g}_i}{\partial x_i^2} \right\| \geq \left\| \frac{\partial^2 \hat{g}_i}{\partial x_i \partial x_j} \right\|$ by assumption from (7) implies that $\frac{\partial^2 \hat{g}_i}{\partial x_i^2} \leq \frac{\partial^2 \hat{g}_i}{\partial x_i \partial x_j} \leq 0$, and by transitivity $\frac{\partial^2 \hat{g}_i}{\partial x_i^2} - \frac{\partial^2 f_i}{\partial y_i^2} \leq \frac{\partial^2 \hat{g}_i}{\partial x_i \partial x_j} \leq 0$. (ii) As $\frac{\partial^2 \hat{g}_j}{\partial x_j^2} < 0$, here $\left\| \frac{\partial^2 \hat{g}_j}{\partial x_j^2} \right\| \geq \left\| \frac{\partial^2 \hat{g}_j}{\partial x_j \partial y_i} \right\|$ by assumption from (6) leads to $\frac{\partial^2 \hat{g}_j}{\partial x_j^2} \leq \frac{\partial^2 \hat{g}_j}{\partial x_j \partial y_i} \leq 0$. From (i) and (ii) we obtain that

$$-\left(\frac{\partial^2 \hat{g}_i}{\partial x_i^2} - \frac{\partial^2 f_i}{\partial y_i^2} \right) \frac{\partial^2 \hat{g}_j}{\partial x_j^2} \leq -\frac{\partial^2 \hat{g}_i}{\partial x_i \partial x_j} \frac{\partial^2 \hat{g}_j}{\partial x_j \partial y_i} \leq 0,$$

with an equality sign (the 1st one) if and only if $\frac{\partial^2 \hat{g}_j}{\partial x_j^2} = \frac{\partial^2 \hat{g}_j}{\partial x_j \partial y_i} < 0$ and $\frac{\partial^2 \hat{g}_i}{\partial x_i^2} - \frac{\partial^2 f_i}{\partial y_i^2} = \frac{\partial^2 \hat{g}_i}{\partial x_i \partial x_j} < 0$. Multiplying through by $\frac{\partial^2 \hat{g}_j}{\partial x_j^2} - \frac{\partial^2 f_j}{\partial y_j^2} < 0$, adding $\frac{\partial^2 \hat{g}_j}{\partial x_j^2} \frac{\partial^2 \hat{g}_j}{\partial x_j \partial y_i} \frac{\partial^2 \hat{g}_i}{\partial x_i \partial y_j}$ on both sides, and reorganizing terms, leads to

$$1 \geq \frac{\frac{\partial^2 \hat{g}_j}{\partial x_j \partial y_i}}{-\frac{\partial^2 \hat{g}_j}{\partial x_j^2}} \frac{N_{jj}}{\Delta},$$

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so that the expression between brackets is non-negative (45) is positive, and finally we have

$$\frac{dy_j^*}{dx_j} = -\frac{-\frac{\partial^2 \hat{g}_j}{\partial x_j^2}}{\frac{\partial^2 \hat{g}_j}{\partial x_j^2} - \frac{\partial^2 f_j}{\partial y_j^2}}\underbrace{\left[1 - \frac{\frac{\partial^2 \hat{g}_j}{\partial x_j \partial y_i}}{-\frac{\partial^2 \hat{g}_i}{\partial x_j^2}}\frac{N_{jj}}{\Delta}\right]}_{\geq 0} \leq 0, \tag{48}$$

$$\underbrace{\phantom{-\frac{-\frac{\partial^2 \hat{g}_j}{\partial x_j^2}}{\frac{\partial^2 \hat{g}_j}{\partial x_j^2} - \frac{\partial^2 f_j}{\partial y_j^2}}}}_{<0}$$

again with an equality sign if and only if $\frac{\partial^2 \hat{g}_j}{\partial x_j^2} = \frac{\partial^2 \hat{g}_j}{\partial x_j \partial y_i} < 0$ and $\frac{\partial^2 \hat{g}_i}{\partial x_i^2} - \frac{\partial^2 f_i}{\partial y_i^2} = \frac{\partial^2 \hat{g}_i}{\partial x_i \partial x_j} < 0$, where the latter equality implies that $\frac{\partial^2 f_i}{\partial y_i^2} = 0$.

Case 3: $\frac{\partial^2 \hat{g}_i}{\partial s_i^2} > 0$ ($i = 1, 2$). Here we have $\left(\frac{\partial^2 \hat{g}_i}{\partial x_i^2} - \frac{\partial^2 f_i}{\partial y_i^2}\right)\frac{\partial^2 \hat{g}_j}{\partial x_j^2} < 0$, which together with $\frac{\partial^2 \hat{g}_j}{\partial x_j \partial y_i}\frac{\partial^2 \hat{g}_i}{\partial x_i \partial x_j} \geq 0$ (partial cross-derivatives have the same sign by assumption) implies that $\left(\frac{\partial^2 \hat{g}_i}{\partial x_i^2} - \frac{\partial^2 f_i}{\partial y_i^2}\right)\frac{\partial^2 \hat{g}_j}{\partial x_j^2} < \frac{\partial^2 \hat{g}_j}{\partial x_j \partial y_i}\frac{\partial^2 \hat{g}_i}{\partial x_i \partial x_j}$. Multiplying through by $\frac{\partial^2 \hat{g}_j}{\partial x_j^2} - \frac{\partial^2 f_j}{\partial y_j^2} < 0$, adding $-\frac{\partial^2 \hat{g}_j}{\partial x_j^2}\frac{\partial^2 \hat{g}_j}{\partial x_j \partial y_i}\frac{\partial^2 \hat{g}_i}{\partial x_i \partial y_j}$ on both sides of the inequality sign, and reorganizing terms, leads to

$$1 > \frac{\frac{\partial^2 \hat{g}_j}{\partial x_j \partial y_i}}{-\frac{\partial^2 \hat{g}_j}{\partial x_j^2}}\frac{N_{jj}}{\Delta}, \tag{49}$$

so that the expression between brackets in (45) is positive. Then $-\frac{\partial^2 \hat{g}_j}{\partial x_j^2}\left(\frac{\partial^2 \hat{g}_j}{\partial x_j^2} - \frac{\partial^2 f_j}{\partial y_j^2}\right)^{-1} > 0$ implies finally that

$$\frac{dy_j^*}{dx_j} = \underbrace{\frac{-\frac{\partial^2 \hat{g}_j}{\partial x_j^2}}{\frac{\partial^2 \hat{g}_j}{\partial x_j^2} - \frac{\partial^2 f_j}{\partial y_j^2}}}_{>0}\underbrace{\left[1 - \frac{\frac{\partial^2 \hat{g}_j}{\partial x_j \partial y_i}}{-\frac{\partial^2 \hat{g}_j}{\partial x_j^2}}\frac{N_{jj}}{\Delta}\right]}_{>0} > 0. \tag{50}$$

The sign of $\frac{dy_j^*}{dx_j}$ in (47), (48) and (50), establishes Proposition 1. ∎

A.3 Lemmas

The technical results introduced in this section are needed to prove Propositions 2, 3, and 4. The first two lemmas establish a connection between properties of $\hat{g}_i(\mathbf{x}, \mathbf{y}) \doteq g_i(x_i + y_i, x_j, y_j, \mathbf{z}^*(\mathbf{x}, \mathbf{y}))$ and $\tilde{g}_i(\mathbf{x}) \doteq \hat{g}_i(\mathbf{x}, \mathbf{y}^*(\mathbf{x})) - f_i(y_i^*(\mathbf{x}))$.

Lemma A.1 *Suppose that $\frac{\partial^2 \hat{g}_i}{\partial x_i^2} \leq 0$, $i = 1, 2$. Then $\frac{d\left[\hat{g}_i\left(x_i + y_i^*, x_j, y_j^*\right) - f_i\left(y_i^*\right)\right]}{dx_j}$, $i, j = 1, 2$, $j \neq i$, has the same sign as $\frac{\partial \hat{g}_i\left(x_i + y_i, x_j, y_j\right)}{\partial x_j}$ and $\frac{\partial \hat{g}_i\left(x_i + y_i, x_j, y_j\right)}{\partial y_j}$.*

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Proof. By the envelope theorem, as $y_i^* \doteq y_i^* \left(x_i, x_j \right)$ maximizes $\hat{g}_i \left(x_i + y_i, x_j, y_j \right) - f_i \left(y_i \right)$, we have

$$\frac{d \left[\hat{g}_i \left(x_i + y_i^*, x_j, y_j^* \right) - f_i \left(y_i^* \right) \right]}{dx_j} = \frac{\partial \hat{g}_i \left(x_i + y_i^*, x_j, y_j^* \right)}{\partial x_j} + \frac{\partial \hat{g}_i \left(x_i + y_i^*, x_j, y_j^* \right)}{\partial y_j} \frac{dy_j^*}{dx_j}. \tag{51}$$

Our objective is to determine the sign of the RHS expression in (51). Given the (same) sign of $\frac{\partial \hat{g}_i \left(x_i + y_i^*, x_j, y_j^* \right)}{\partial x_j}$ and $\frac{\partial \hat{g}_i \left(x_i + y_i^*, x_j, y_j^* \right)}{\partial y_j}$, we need only characterizing $\frac{dy_j^*}{dx_j}$.

First, if $\frac{\partial^2 \hat{g}_i}{\partial x_i^2} = 0$ ($i = 1, 2$), we know from (47) that $\frac{dy_j^*}{dx_j} = 0$, which is sufficient to conclude.

Next, if $\frac{\partial^2 \hat{g}_i}{\partial x_i^2} < 0$ ($i = 1, 2$), we know from (48) that $\frac{dy_j^*}{dx_j} \leq 0$. Then toward a contradiction we suppose that $\left\| \frac{dy_j^*}{dx_j} \right\| > 1$, or equivalently here $\frac{dy_j^*}{dx_j} < -1$. Developing the expression in (45) then leads to

$$\frac{\partial^2 \hat{g}_j}{\partial x_j \partial y_i} \left(\frac{\partial^2 \hat{g}_i}{\partial x_i \partial y_j} - \frac{\partial^2 \hat{g}_i}{\partial x_i \partial x_j} \right) > -\underbrace{\frac{\partial^2 f_j}{\partial y_j^2}}_{\geq 0} \underbrace{\left(\frac{\partial^2 \hat{g}_i}{\partial x_i^2} - \frac{\partial^2 f_i \left(y_i^* \right)}{\partial y_i^2} \right)}_{<0}. \tag{52}$$

As $\frac{\partial^2 \hat{g}_i}{\partial x_i \partial y_j}$ and $\frac{\partial^2 \hat{g}_i}{\partial x_i \partial x_j}$ have the same sign, and $\left\| \frac{\partial^2 \hat{g}_i}{\partial x_i \partial x_j} \right\| \geq \left\| \frac{\partial^2 \hat{g}_i}{\partial x_i \partial y_j} \right\|$ (model specifications in (6-7)), we know that the expression on the LHS of the strict inequality sign in (57) is non-positive. However, $\frac{\partial^2 f_j}{\partial y_j^2} \geq 0$ (by assumption) and $\frac{\partial^2 \hat{g}_i}{\partial x_i^2} - \frac{\partial^2 f_i \left(y_i^* \right)}{\partial y_i^2} < 0$ (second-order condition) imply that the product on the RHS is always non-negative, a contradiction. Hence $\left\| \frac{dy_j^*}{dx_j} \right\| \leq 1$. This, together with $\left\| \frac{\partial \hat{g}_i \left(x_i + y_i^*, x_j, y_j^* \right)}{\partial x_j} \right\| \geq \left\| \frac{\partial \hat{g}_i \left(x_i + y_i^*, x_j, y_j^* \right)}{\partial y_j} \right\|$ (model specifications), is sufficient to conclude that $\frac{d \left[\hat{g}_i \left(x_i + y_i^*, x_j, y_j^* \right) - f_i \left(y_i^* \right) \right]}{dx_j}$ in (51) has the same sign as $\frac{\partial \hat{g}_i \left(x_i + y_i, x_j, y_j \right)}{\partial x_j}$ and $\frac{\partial \hat{g}_i \left(x_i + y_i, x_j, y_j \right)}{\partial y_j}$. ∎

Lemma A.2 *Suppose that $\frac{\partial^2 \hat{g}_i}{\partial x_i^2} \leq 0$, $i = 1, 2$. If $\frac{\partial \hat{g}_i \left(x_i + y_i, x_j, y_j \right)}{\partial x_j} \geq 0$ and $\frac{\partial \hat{g}_i \left(x_i + y_i, x_j, y_j \right)}{\partial y_j} \geq 0$, $i, j = 1, 2$, $j \neq i$, then $\frac{d \left[\hat{g}_i \left(x_i + y_i^*, x_j, y_j^* \right) - f_i \left(y_i^* \right) \right]}{dx_i} \geq 0$ also.*

Proof. By the envelope theorem, as $y_i^* \doteq y_i^* \left(x_i, x_j \right)$ maximizes $\hat{g}_i \left(x_i + y_i, x_j, y_j \right) - f_i \left(y_i \right)$, we have

$$\frac{d \left[\hat{g}_i \left(x_i + y_i^*, x_j, y_j^* \right) - f_i \left(y_i^* \right) \right]}{dx_i} = \frac{\partial \hat{g}_i \left(x_i + y_i^*, x_j, y_j^* \right)}{\partial x_i} + \frac{\partial \hat{g}_i \left(x_i + y_i^*, x_j, y_j^* \right)}{\partial y_j} \frac{dy_j^*}{dx_i}, \tag{53}$$

where $\frac{\partial \hat{g}_i \left(x_i + y_i^*, x_j, y_j^* \right)}{\partial x_i} \geq 0$ as a model specification, and $\frac{\partial \hat{g}_i \left(x_i + y_i^*, x_j, y_j^* \right)}{\partial y_j} \geq 0$ as an assumption of the present lemma. In order to determine the sign of the RHS expression in (53), we thus need only characterizing $\frac{dy_j^*}{dx_i}$.

First, if $\frac{\partial^2 \hat{g}_i}{\partial x_i^2} = 0$ ($i = 1, 2$), we know from (47) that $\frac{dy_j^*}{dx_i} = 0$, which is sufficient to conclude.

Next, if $\frac{\partial^2 \hat{g}_i}{\partial x_i^2} < 0$ ($i = 1, 2$), recall from (46) in Section A.1 that

$$\frac{dy_j^*}{dx_i} = \frac{-\frac{\partial^2 \hat{g}_j}{\partial x_j \partial x_i}}{\frac{\partial^2 \hat{g}_j}{\partial x_j^2} - \frac{\partial^2 f_j}{\partial y_j^2}} \left[1 - \frac{\frac{\partial^2 \hat{g}_j}{\partial x_j \partial y_i}}{-\frac{\partial^2 \hat{g}_j}{\partial x_j \partial x_i}} \frac{N_{ji}}{\Delta} \right], \tag{54}$$

where $N_{ji} \doteq \frac{\partial^2 \hat{g}_i}{\partial x_i \partial y_j} \frac{\partial^2 \hat{g}_j}{\partial x_j \partial x_i} - \left(\frac{\partial^2 \hat{g}_j}{\partial x_j^2} - \frac{\partial^2 f_j}{\partial y_j^2} \right) \frac{\partial^2 \hat{g}_i}{\partial x_i^2}$. There are two possible cases that depend on the sign of $\frac{\partial^2 \hat{g}_j}{\partial x_j \partial x_i}$.

(i) If $\frac{\partial^2 \hat{g}_j}{\partial x_j \partial x_i} \geq 0$ ($i, j = 1, 2, j \neq i$), as $\frac{\partial^2 \hat{g}_j}{\partial x_j^2} - \frac{\partial^2 f_j}{\partial y_j^2} < 0$ we have $-\frac{\partial^2 \hat{g}_j}{\partial x_j \partial x_i} / \left(\frac{\partial^2 \hat{g}_j}{\partial x_j^2} - \frac{\partial^2 f_j}{\partial y_j^2} \right) \geq 0$. Then, toward a contradiction, suppose that the expression between brackets in (54) is negative. This, together with $\left\| \frac{\partial^2 \hat{g}_j}{\partial x_j \partial y_i} / \frac{\partial^2 \hat{g}_j}{\partial x_j \partial x_i} \right\| \leq 1$ (model specifications in (6-7)), implies that $\frac{N_{ji}}{\Delta} < -1$, which can be rewritten as

$$\frac{\partial^2 \hat{g}_i}{\partial x_i \partial y_j} \left(\frac{\partial^2 \hat{g}_j}{\partial x_j \partial x_i} - \frac{\partial^2 \hat{g}_j}{\partial x_j \partial y_i} \right) < \frac{\partial^2 f_i}{\partial y_i^2} \left(\frac{\partial^2 \hat{g}_j}{\partial x_j^2} - \frac{\partial^2 f_j}{\partial y_j^2} \right),$$

where the expression on the LHS of the inequality sign is non-negative, whereas the expression on the RHS is non-positive, a contradiction. It follows that $\frac{dy_j^*}{dx_i} \geq 0$, which is sufficient to conclude directly that $\frac{d \left[\hat{g}_i \left(x_i + y_i^*, x_j, y_j^* \right) - f_i \left(y_i^* \right) \right]}{dx_i}$ in (53) is non-negative also.

(ii) If $\frac{\partial^2 \hat{g}_j}{\partial x_j \partial x_i} < 0$ ($i, j = 1, 2, j \neq i$), unlike in the previous case the model specifications do not imply that $\frac{dy_j^*}{dx_i} \geq 0$. Then, toward a contradiction, whenever $\frac{dy_j^*}{dx_i} < 0$ suppose that $\left\| \frac{dy_j^*}{dx_i} \right\| > 1$, or equivalently here $-\frac{dy_j^*}{dx_i} > 1$. From (54), by using $\Delta > 0$ (see (41) and related subsequent comments in Section A.1) we have

$$\frac{-\frac{\partial^2 \hat{g}_j}{\partial x_j \partial y_i} \frac{\partial^2 \hat{g}_i}{\partial x_i^2} + \frac{\partial^2 \hat{g}_j}{\partial x_j \partial x_i} \left(\frac{\partial^2 \hat{g}_i}{\partial x_i^2} - \frac{\partial^2 f_i}{\partial y_i^2} \right)}{\left(\frac{\partial^2 \hat{g}_i}{\partial x_i^2} - \frac{\partial^2 f_i}{\partial y_i^2} \right) \left(\frac{\partial^2 \hat{g}_j}{\partial x_j^2} - \frac{\partial^2 f_j}{\partial y_j^2} \right) - \frac{\partial^2 \hat{g}_i}{\partial x_i \partial y_j} \frac{\partial^2 \hat{g}_j}{\partial x_j \partial y_i}} > 1,$$

which can be rewritten as

$$-\frac{\partial^2 \hat{g}_j}{\partial x_j \partial y_i} \frac{\partial^2 \hat{g}_i}{\partial x_i^2} + \frac{\partial^2 \hat{g}_j}{\partial x_j \partial x_i} \left(\frac{\partial^2 \hat{g}_i}{\partial x_i^2} - \frac{\partial^2 f_i}{\partial y_i^2} \right) > \left(\frac{\partial^2 \hat{g}_i}{\partial x_i^2} - \frac{\partial^2 f_i}{\partial y_i^2} \right) \left(\frac{\partial^2 \hat{g}_j}{\partial x_j^2} - \frac{\partial^2 f_j}{\partial y_j^2} \right) - \frac{\partial^2 \hat{g}_i}{\partial x_i \partial y_j} \frac{\partial^2 \hat{g}_j}{\partial x_j \partial y_i},$$

with $\frac{\partial^2 \hat{g}_i}{\partial x_i^2}$ and $\frac{\partial^2 \hat{g}_i}{\partial x_i \partial y_j}$ both negative here. Moreover we know by assumption from (7) that $\left\| \frac{\partial^2 \hat{g}_i}{\partial x_i^2} \right\| \geq \left\| \frac{\partial^2 \hat{g}_i}{\partial x_i \partial y_j} \right\|$. Therefore, substituting $\frac{\partial^2 \hat{g}_i}{\partial x_i^2}$ for $\frac{\partial^2 \hat{g}_i}{\partial x_i \partial y_j}$ in the last term above, by transitivity we obtain

$$-\frac{\partial^2 \hat{g}_j}{\partial x_j \partial y_i} \frac{\partial^2 \hat{g}_i}{\partial x_i^2} + \frac{\partial^2 \hat{g}_j}{\partial x_j \partial x_i} \left(\frac{\partial^2 \hat{g}_i}{\partial x_i^2} - \frac{\partial^2 f_i}{\partial y_i^2} \right) > \left(\frac{\partial^2 \hat{g}_i}{\partial x_i^2} - \frac{\partial^2 f_i}{\partial y_i^2} \right) \left(\frac{\partial^2 \hat{g}_j}{\partial x_j^2} - \frac{\partial^2 f_j}{\partial y_j^2} \right) - \frac{\partial^2 \hat{g}_j}{\partial x_j \partial y_i} \frac{\partial^2 \hat{g}_i}{\partial x_i^2},$$

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which simplifies to

$$\frac{\partial^2 \hat{g}_j}{\partial x_j \partial x_i} < \frac{\partial^2 \hat{g}_j}{\partial x_j^2} - \frac{\partial^2 f_j}{\partial y_j^2} \leq \frac{\partial^2 \hat{g}_j}{\partial x_j^2} \leq 0.$$

As the latter inequalities contradict the initial assumption in (6) that $\left\| \frac{\partial^2 \hat{g}_j}{\partial x_j \partial x_i} \right\| \leq \left\| \frac{\partial^2 \hat{g}_j}{\partial x_j^2} \right\|$, it must be

the case that $\left\| \frac{dy_j^*}{dx_i} \right\| \leq 1$. This, together with the model specification in (4-5) that $\left\| \frac{\partial \hat{g}_i (x_i + y_i^*, x_j, y_j^*)}{\partial x_i} \right\| \geq$

$\left\| \frac{\partial \hat{g}_i (x_i + y_i^*, x_j, y_j^*)}{\partial y_j} \right\|$, is sufficient to conclude that $\frac{d[\hat{g}_i (x_i + y_i^*, x_j, y_j^*) - f_i(y_i^*)]}{dx_i}$ in (53) is non-negative. ∎

The next two lemmas were established in Laussel and Le Breton (2001). We restate them in the notation of this paper for a self-contained appendix:[49]

Lemma A.3 *If v is superadditive, that is $\Lambda \geq v(\{1\}) + v(\{2\})$, then in all TSPNE $v_0^* = 0$, and all vectors of equilibrium profits (v_1^*, v_2^*) are such that $v_1^* + v_2^* = \Lambda$.*

Lemma A.4 *If v is strictly subadditive, that is $\Lambda < v(\{1\}) + v(\{2\})$, then in all TSPNE $v_0^* > 0$, and there exists a unique vector of equilibrium profits (v_1^*, v_2^*), where $v_i^* = \Lambda - v(\{j\})$, $i, j = 1, 2, j \neq i$.*

A.4 Proof of Propositions 2, 3, and 4.

Proof of Proposition 2. We first use Lemmas A.1 and A.2, and finally Lemma A.3, in order to extend a proof by Billette de Villemeur and Versaevel (2003, Proposition 1) to establish the (weak) superadditivity of $v(.)$. Then we show that the equilibrium payoffs (v_1^*, v_2^*) exist that are (weakly) higher than the respective standalone values $(\underline{v}_1, \underline{v}_2)$.

1) Denote by $X_{\{i\}}^*$ the set of R&D levels that maximize the joint profit of firm i and the lab, that is

$$X_{\{i\}}^* = \arg \max_{\mathbf{x}} \left(\max_{y_i} \left[\hat{g}_i \left(x_i + y_i, x_j, y_j \right) - f_i \left(y_i \right) \right] - f_0 \left(\mathbf{x} \right) \right).$$

Define $\mathbf{a} \doteq (a_1, a_2) \in X_{\{1\}}^*$ and $\mathbf{b} \doteq (b_1, b_2) \in X_{\{2\}}^*$.

We know from the initial model specifications that $\frac{\partial \hat{g}_i (x_i + y_i, x_j, y_j)}{\partial s_i} \geq 0$, where $s_i = x_i + y_i$. More-over, it is assumed in this proposition that $\frac{\partial^2 \hat{g}_i}{\partial x_i^2} \leq 0$ (non-increasing returns to R&D), and from (13) that $\frac{\partial \hat{g}_i (x_i + y_i, x_j, y_j)}{\partial x_j} \geq 0$ and $\frac{\partial \hat{g}_i (x_i + y_i, x_j, y_j)}{\partial y_j} \geq 0$ (non-negative R&D externalities). It follows that $\hat{g}_i (x_i + y_i^* (\mathbf{x}), x_j, y_j^* (\mathbf{x})) - f_i (y_i^* (\mathbf{x}))$ is non-decreasing in x_j from Lemma A.1, and also in x_i from

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Lemma A.2. Therefore, for $\mathbf{s} \doteq (s_1, s_2)$, with $s_1 \doteq a_1 \vee b_1$ and $s_2 \doteq a_2 \vee b_2$, we have

$$\hat{g}_1\left(a_1 + y_1^*(\mathbf{a}), a_2, y_2^*(\mathbf{a})\right) - f_1\left(y_1^*(\mathbf{a})\right) \leq \hat{g}_1\left(s_1 + y_1^*(\mathbf{s}), s_2, y_2^*(\mathbf{s})\right) - f_1\left(y_1^*(\mathbf{s})\right), \quad (55a)$$

$$\hat{g}_2\left(b_2 + y_2^*(\mathbf{b}), b_1, y_1^*(\mathbf{b})\right) - f_2\left(y_2^*(\mathbf{b})\right) \leq \hat{g}_2\left(s_2 + y_2^*(\mathbf{s}), s_1, y_1^*(\mathbf{s})\right) - f_2\left(y_2^*(\mathbf{s})\right). \quad (55b)$$

The non-negative cross-derivative in (12) implies the weak submodularity of f_0 (Topkis, 1995). This property, with (55a) and (55b), together lead to

$$\underbrace{\hat{g}_1\left(a_1 + y_1^*(\mathbf{a}), a_2, y_2^*(\mathbf{a})\right) - f_1\left(y_1^*(\mathbf{a})\right) - f_0(\mathbf{a})}_{=v(\{1\})} + \underbrace{\hat{g}_2\left(b_2 + y_2^*(\mathbf{b}), b_1, y_1^*(\mathbf{b})\right) - f_2\left(y_1^*(\mathbf{b})\right) - f_0(\mathbf{b})}_{=v(\{2\})}$$

$$\leq \underbrace{\hat{g}_1\left(s_1 + y_1^*(\mathbf{s}), s_2, y_2^*(\mathbf{s})\right) - f_1\left(y_1^*(\mathbf{s})\right) + \hat{g}_2\left(s_2 + y_2^*(\mathbf{s}), s_1, y_1^*(\mathbf{s})\right) - f_2\left(y_2^*(\mathbf{s})\right) - f_0(\mathbf{s})}_{\leq v(\{1,2\})} - \underbrace{f_0(\mathbf{a} \wedge \mathbf{b})}_{\geq 0},$$

which in turn establishes that $v(\{1\}) + v(\{2\}) \leq v(\{1,2\})$. Then the conclusion that $v_0^* = 0 < v_1^* + v_2^* = v(\{1,2\})$ follows directly from Lemma A.3.

2) To check that $v_i^* \geq \underline{v}_i$, recall that firm i's standalone value $\underline{v}_i \doteq \tilde{g}_j(\mathbf{x}_{\{j\}}^*)$, where $\mathbf{x}_{\{j\}}^* \in \arg\max_{\mathbf{x}}[\tilde{g}_j(\mathbf{x}) - f_0(\mathbf{x})]$, is the R&D outcomes when firm j is assumed to have exclusive access to the lab (for $i, j = 1, 2$, $j \neq i$). Moreover, by assumption firm i's exclusive control of the lab dominates the standalone value, that is $v(\{i\}) \geq \underline{v}_i$. Then from the superadditivity of $v(.)$, together with $v_1^* + v_2^* = v(\{1,2\})$ as established above, we have directly

$$\underline{v}_1 + \underline{v}_2 \leq v(\{1\}) + v(\{2\}) \leq v(\{1,2\}) = v_1^* + v_2^*,$$

and the equilibrium set $\left\{ (v_1^*, v_2^*) \mid v_1^* + v_2^* = \Lambda,\ v_1^* \geq \underline{v}_1,\ v_2^* \geq \underline{v}_2 \right\}$ is nonempty. ∎

Proof of Proposition 3. We first use Lemmas A.1 and A.4 to prove the strict subadditivity of $v(.)$, before establishing that the equilibrium payoffs (v_1^*, v_2^*) are (weakly) higher than the respective standalone values $(\underline{v}_1, \underline{v}_2)$.

1) Pick any $\mathbf{x}^* \doteq (x_1^*, x_2^*)$ in $X_{\{1,2\}}^*$, the set of R&D levels that maximize industry profits.

It is assumed in this proposition that $\frac{\partial^2 \hat{g}_i}{\partial x_i^2} \leq 0$ (non-increasing returns to R&D), and from (17) that that $\frac{\partial \hat{g}_i(x_i + y_i, x_j, y_j)}{\partial x_j} \leq 0$ and $\frac{\partial \hat{g}_i(x_i + y_i, x_j, y_j)}{\partial y_j} \leq 0$ (weakly negative R&D externalities). It follows from Lemma A.1 that the net profit expression $\hat{g}_i(x_i + y_i^*(\mathbf{x}), x_j, y_j^*(\mathbf{x})) - f_i(y_i^*(\mathbf{x}))$ is non-decreasing so that, for all $x_1^*, x_2^* \geq 0$,

$$\hat{g}_1\left(x_1^* + y_1^*(\mathbf{x}^*), x_2^*, y_2^*(\mathbf{x}^*)\right) - f_1\left(y_1^*(\mathbf{x}^*)\right) \leq \hat{g}_1\left(x_1^* + y_1^*(x_1^*, 0), 0, y_2^*(x_1^*, 0)\right) - f_1\left(y_1^*(x_1^*, 0)\right), \quad (56a)$$

$$\hat{g}_2\left(x_2^* + y_2^*(\mathbf{x}^*), x_1^*, y_1^*(\mathbf{x}^*)\right) - f_2\left(y_2^*(\mathbf{x}^*)\right) \leq \hat{g}_2\left(x_2^* + y_2^*(0, x_2^*), 0, y_1^*(0, x_2^*)\right) - f_2\left(y_2^*(0, x_2^*)\right). \quad (56b)$$

The negative cross-derivative in (16) implies the strict supermodularity of f_0 (Topkis, 1995), with $f_0(0,0) = 0$. This property, together with (56a) and (56b), lead to

$$\underbrace{\hat{g}_1(x_1^* + y_1^*(\mathbf{x}^*), x_2^*, y_2^*(\mathbf{x}^*)) - f_1(y_1^*(\mathbf{x}^*)) + \hat{g}_2(x_2^* + y_2^*(\mathbf{x}^*), x_1^*, y_1^*(\mathbf{x}^*)) - f_2(y_2^*(\mathbf{x}^*)) - f_0(x_1^*, x_2^*)}_{=v(\{1,2\})}$$

$$< \underbrace{\hat{g}_1(x_1^* + y_1^*(x_1^*, 0), 0, y_2^*(x_1^*, 0)) - f_1(y_1^*(x_1^*, 0)) - f_0(x_1^*, 0)}_{\leq v(\{1\})}$$

$$+ \underbrace{\hat{g}_2(x_2^* + y_2^*(0, x_2^*), 0, y_1^*(0, x_2^*)) - f_2(y_2^*(0, x_2^*)) - f_0(0, x_2^*)}_{\leq v(\{2\})},$$

which establishes that $v(\{1,2\}) < v(\{1\}) + v(\{2\})$. Then the conclusion that $v_0^* > 0$ and $v_i^* = \Lambda - v(\{j\})$, $i,j = 1,2$, $j \neq i$, follows directly from Lemma A.4.

2) For any $\mathbf{x}_{\{1\}}^*$ and $\mathbf{x}_{\{2\}}^*$, by definition of $v(.)$ we have

$$\tilde{g}_1(\mathbf{x}_{\{1\}}^*) + \tilde{g}_2(\mathbf{x}_{\{1\}}^*) - f_0(\mathbf{x}_{\{1\}}^*) \leq v(\{1,2\}),$$
$$\tilde{g}_1(\mathbf{x}_{\{2\}}^*) + \tilde{g}_2(\mathbf{x}_{\{2\}}^*) - f_0(\mathbf{x}_{\{2\}}^*) \leq v(\{1,2\}).$$

Then by reorganizing terms, and recalling that $v(\{i\}) \doteq \tilde{g}_i(\mathbf{x}_{\{i\}}^*) - f_0(\mathbf{x}_{\{i\}}^*)$ and $\underline{v}_i \doteq \tilde{g}_i(\mathbf{x}_{\{j\}}^*)$, where $\mathbf{x}_{\{j\}}^* \in \arg\max_{\mathbf{x}} [\tilde{g}_j(\mathbf{x}) - f_0(\mathbf{x})]$, $i,j = 1,2$, $j \neq i$, we obtain

$$v(\{1\}) + \underline{v}_2 \leq v(\{1,2\}),$$
$$v(\{2\}) + \underline{v}_1 \leq v(\{1,2\}),$$

which, together with $v_i^* = \Lambda - v(\{j\})$, $i,j = 1,2$, $j \neq i$, as established above, implies that $\underline{v}_i \leq v_i^*$. ∎

Proof of Proposition 4. First, Lemma A.1 extends to the case $\frac{\partial^2 \hat{g}_i}{\partial x_i^2} \geq 0$ ($i = 1,2$). Indeed we have established in (47) that $\frac{\partial^2 \hat{g}_i}{\partial x_i^2} = 0 \Rightarrow \frac{dy_j^*}{dx_j} = 0$, and in (50) that $\frac{\partial^2 \hat{g}_i}{\partial x_i^2} > 0 \Rightarrow \frac{dy_j^*}{dx_j} > 0$. This is sufficient to conclude directly that $\frac{d[\hat{g}_i(x_i + y_i^*(\mathbf{x}), x_j, y_j^*(\mathbf{x})) - f_i(y_i^*(\mathbf{x}))]}{dx_j}$ in (51) has the same sign as $\frac{\partial \hat{g}_i(x_i + y_i, x_j, y_j)}{\partial x_j}$ and $\frac{\partial \hat{g}_i(x_i + y_i, x_j, y_j)}{\partial y_j}$.

To extend Lemma A.2 as well, note that $\frac{\partial^2 \hat{g}_i}{\partial x_i^2} \geq 0$ ($i = 1,2$) implies $\frac{N_{ji}}{\Delta} \geq 0$ in (54), because $\Delta > 0$ (from stability condition) and $N_{ji} \geq 0$ from $\frac{\partial^2 \hat{g}_j}{\partial x_j^2} - \frac{\partial^2 f_j}{\partial y_j^2} < 0$ (second-order condition) and $\frac{\partial^2 \hat{g}_i}{\partial x_j^2} \geq 0$ (assumption in this proposition). Then there are only two possible cases:

(i) If $\frac{\partial^2 \hat{g}_j}{\partial x_j \partial x_i} \geq 0$ then $\frac{\partial^2 \hat{g}_j}{\partial x_j \partial y_i} \geq 0$ also (model specifications). As $\frac{N_{ji}}{\Delta} \geq 0$, we obtain that the expression between brackets in (54) is positive. Moreover, $\frac{\partial^2 \hat{g}_j}{\partial x_j^2} - \frac{\partial^2 f_j}{\partial y_j^2} < 0$ (second-order condition) here implies

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that $-\frac{\partial^2 \hat{g}_j}{\partial x_j \partial x_i} \left(\frac{\partial^2 \hat{g}_j}{\partial x_j^2} - \frac{\partial^2 f_j}{\partial y_j^2} \right)^{-1} \geq 0$. Therefore, from (54) we have $\frac{dy_j^*}{dx_i} \geq 0$, which is sufficient to conclude

directly that $\frac{d\left[\hat{g}_i\left(x_i + y_i^*(\mathbf{x}), x_i, y_j^*(\mathbf{x}) \right) - f_i\left(y_i^*(\mathbf{x}) \right) \right]}{dx_i}$ in (53) is non-negative also.

(ii) If $\frac{\partial^2 \hat{g}_j}{\partial x_j \partial x_i} \leq 0$ then $\frac{\partial^2 \hat{g}_j}{\partial x_j \partial y_i} \leq 0$ also (model specifications). As $\frac{N_{ji}}{\Delta} \geq 0$, again the expression between

brackets in (54) is positive. Moreover, $\frac{\partial^2 \hat{g}_j}{\partial x_j^2} - \frac{\partial^2 f_j}{\partial y_j^2} < 0$ (second-order condition) implies here that

$-\frac{\partial^2 \hat{g}_j}{\partial x_j \partial x_i} \left(\frac{\partial^2 \hat{g}_j}{\partial x_j^2} - \frac{\partial^2 f_j}{\partial y_j^2} \right)^{-1} \leq 0$. Therefore, from (54) we have that $\frac{dy_j^*}{dx_i} \leq 0$, implying that $\left\| \frac{dy_j^*}{dx_i} \right\| = -\frac{dy_j^*}{dx_i}$.

So, recalling that $\left\| \frac{\partial \hat{g}_i}{\partial x_j} \right\| \geq \left\| \frac{\partial \hat{g}_i}{\partial y_j} \right\|$ (model specifications in (6-7)), a sufficient condition for Lemma A.2

to be robust to the increasing R&D return specification is $\frac{dy_j^*}{dx_i} > -1$. ∎

A.5   Proof of industry profit maximization result in Proposition 5.

Recall from the model specifications in Section 3 that, in equilibrium, for any given pair of transfer payment functions $(\tilde{t}_1, \tilde{t}_2)$ we know that $\tilde{\mathbf{x}}$ is an element of $X(\tilde{t}_1, \tilde{t}_2) \doteq \arg\max_{\mathbf{x}} v_0((\mathbf{x}(\tilde{t}_1, \tilde{t}_2)))$, the set of external R&D choices that maximize the lab's profit. We want to demonstrate that $\tilde{\mathbf{x}}$ is also an element of $X_{\{1,2\}}^* \doteq \arg\max_{\mathbf{x}}(\tilde{g}_1(\mathbf{x}) + \tilde{g}_2(\mathbf{x}) - f_0(\mathbf{x}))$, the set of external R&D levels that maximize industry profit. The proof is a simple adaptation, in the notation of our model, of a common agency efficiency result in Bernheim and Whinston (1986b, Theorem 2, p. 14).

We suppose that $\tilde{\mathbf{x}} \notin X_{\{1,2\}}^*$, and look for a contradiction. In equilibrium the strategy $\tilde{t}_i$ is truthful relative to $\tilde{\mathbf{x}}$, that is $\tilde{t}_i(\mathbf{x}) = \sup\{0, \tilde{g}_i(\mathbf{x}) - [\tilde{g}_i(\tilde{\mathbf{x}}) - \tilde{t}_i(\tilde{\mathbf{x}})]\}$, implying that

$$\tilde{g}_i(\mathbf{x}) - \tilde{g}_i(\tilde{\mathbf{x}}) + \tilde{t}_i(\tilde{\mathbf{x}}) \leq \tilde{t}_i(\mathbf{x}),$$

for all $\mathbf{x}$. This holds in particular for any given $\mathbf{x}^* \in X_{\{1,2\}}^*$, so that $\tilde{g}_i(\mathbf{x}^*) - \tilde{g}_i(\tilde{\mathbf{x}}) + \tilde{t}_i(\tilde{\mathbf{x}}) \leq \tilde{t}_i(\mathbf{x}^*)$, $i = 1, 2$. Summing the latter inequality for the two firms, and subtracting $f_0(\mathbf{x}^*)$ on each side, leads to

$$\tilde{g}(\mathbf{x}^*) - \tilde{g}(\tilde{\mathbf{x}}) + \tilde{t}(\tilde{\mathbf{x}}) - f_0(\mathbf{x}^*) \leq \tilde{t}(\mathbf{x}^*) - f_0(\mathbf{x}^*),$$

where $\tilde{g}(\mathbf{x}) \doteq \tilde{g}_1(\mathbf{x}) + \tilde{g}_2(\mathbf{x})$, and $\tilde{t}(\mathbf{x}) \doteq \tilde{t}_1(\mathbf{x}) + \tilde{t}_2(\mathbf{x})$. By introducing $f_0(\tilde{\mathbf{x}})$ on the left-hand side only, and reorganizing terms, we obtain

$$[\tilde{g}(\mathbf{x}^*) - f_0(\mathbf{x}^*)] - [\tilde{g}(\tilde{\mathbf{x}}) - f_0(\tilde{\mathbf{x}})] + \tilde{t}(\tilde{\mathbf{x}}) - f_0(\tilde{\mathbf{x}}) \leq \tilde{t}(\mathbf{x}^*) - f_0(\mathbf{x}^*). \tag{57}$$

Observe that $\mathbf{x}^* \in X_{\{1,2\}}^*$ and $\tilde{\mathbf{x}} \notin X_{\{1,2\}}^*$ together imply that $\tilde{g}(\mathbf{x}^*) - f_0(\mathbf{x}^*) > \tilde{g}(\tilde{\mathbf{x}}) - f_0(\tilde{\mathbf{x}})$, which in turn implies from (57) that $\tilde{t}(\tilde{\mathbf{x}}) - f_0(\tilde{\mathbf{x}}) < \tilde{t}(\mathbf{x}^*) - f_0(\mathbf{x}^*)$. The latter comparison says that $\tilde{\mathbf{x}} \notin X(\tilde{t}_1, \tilde{t}_2)$, a contradiction. Therefore, $\tilde{\mathbf{x}} \in X_{\{1,2\}}^*$. ∎

A.6 Proof of $v_0^{\{0,1\}} = v_0^{\{0,2\}} \geq v_0^* = |\epsilon| > 0$ in Proposition 6 (for $\epsilon < 0$).

Consider the negative technological externalities case ($\epsilon < 0$), with firm i facing two alternatives: if it is the one that acquires the lab, as an integrated entity it earns $\Lambda - v_j^{\{0,i\}}$; otherwise, as an outsider firm it earns $v_i^{\{0,j\}}$. The difference of the latter two payoffs is firm i's willingness to pay for the lab, which is equal to the one of firm j. Therefore, competition for the acquisition of the lab implies that in equilibrium $v_0^{\{0,i\}} = v_0^{\{0,j\}} = \Lambda - v_1^{\{0,2\}} - v_2^{\{0,1\}}$.

Suppose now that firm i is the one that acquires the lab, while firm j remains independent, $i, j = 1, 2$, $j \neq i$. In the latter industry structure, the integrated entity $\{0, i\}$ and firm j bargain over the value generated by the acquired lab, with respective disagreement payoffs $v(\{i\})$ and $\underline{v}_j$. Firm j's payoff is thus

$$v_j^{\{0,i\}} = \underline{v}_j + w_j \left(\Lambda - \underline{v}_j - v(\{i\}) \right), \tag{58}$$

where from (29) firm j's bargaining power is

$$w_j = \frac{v_j^{\{1,2\}} - v_j^*}{\Lambda - v_1^* - v_2^*}. \tag{59}$$

Given that $v_0^{\{0,i\}} = \Lambda - v_1^{\{0,2\}} - v_2^{\{0,1\}}$, as established above, and using (58-59), we have

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

which, by reorganizing terms, can be rewritten as

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

Then, recalling that $v_0^* = |\epsilon| = v(\{1\}) + v(\{2\}) - \Lambda$, and that $\Lambda = v_1^{\{1,2\}} + v_2^{\{1,2\}}$, after a few steps we obtain that $v_0^{\{0,1\}} \geq v_0^*$ if and only if

$$\left(\frac{v(\{1\}) - v_1^{\{1,2\}}}{|\epsilon|} \right) [\underline{v}_1 + v(\{2\}) - \Lambda] + \left(\frac{v(\{2\}) - v_2^{\{1,2\}}}{|\epsilon|} \right) [\underline{v}_2 + v(\{1\}) - \Lambda] \leq 0. \tag{60}$$

As the two added terms in (60) are symmetric, we focus on the first one:

(i) Consider the expression between square brackets. By definition of $\Lambda \doteq \max_{\mathbf{x}} (\tilde{g}_1(\mathbf{x}) + \tilde{g}_2(\mathbf{x}) - f_0(\mathbf{x}))$, we have $\Lambda \geq \tilde{g}_1(\mathbf{x}_{\{2\}}^*) + \tilde{g}_2(\mathbf{x}_{\{2\}}^*) - f_0(\mathbf{x}_{\{2\}}^*)$, where $\mathbf{x}_{\{2\}}^* \in \arg\max_{\mathbf{x}}[\tilde{g}_2(\mathbf{x}) - f_0(\mathbf{x})]$. Since $\underline{v}_1 = \tilde{g}_1(\mathbf{x}_{\{2\}}^*)$ and $v(\{2\}) = \tilde{g}_2(\mathbf{x}_{\{2\}}^*) - f_0(\mathbf{x}_{\{2\}}^*)$, we have $\underline{v}_1 + v(\{2\}) - \Lambda \leq 0$.

(ii) Consider the numerator in the term between parentheses. From Proposition 3 we know that

$v_2^* = \Lambda - v(\{1\})$. Moreover, $\Lambda - v_1^* - v_2^* = v_0^* > 0$ implies from (28) that $v_2^{\{1,2\}} > v_2^*$ for all (ω_1, ω_2) in $(0,1)^2$. It follows that $v_2^{\{1,2\}} > \Lambda - v(\{1\})$, and it is sufficient to recall that $v_2^{\{1,2\}} = \Lambda - v_1^{\{1,2\}}$ (the lab makes no profit in the horizontal arrangement) to establish that $v(\{1\}) - v_1^{\{1,2\}} > 0$.

Therefore, (60) is always true, with a strict inequality sign whenever $\Lambda > \tilde{g}_i(\mathbf{x}_{\{i\}}^*) + \tilde{g}_j(\mathbf{x}_{\{i\}}^*) - f_0(\mathbf{x}_{\{i\}}^*)$, for some $i = 1, 2, j \neq i$. $\blacksquare$