FAST-TRACK R→D 4 PARTNERING WITH FRANCE

LYONBIOPOLE

MEDICEN PARIS REGION

ALSACE BIOVALLEY

EUROBIOMED

ATLANPOLE BIOTHERAPIES

NUTRITION HEALTHCARE LONGEVITY CLUSTER

CANCER-BIO-HEALTH CLUSTER

PROD'INNOV

# Bio-Modeling Systems

Manuel GEA, Co-founder & CEO,

BIO-MODELING SYSTEMS:

A leading Integrative Systems Biology SME.

New collaborative R&D paradigm deciphered. Set-up background

First operational successes in CNS, biodefense/biosecurity and Green Industrial Biotech.

PHERECYDES PHARMA

Bio·IT World Best Practices AWARD Honorable Mention 2009

Synthons

BM Systems

cea

## INTERNATIONAL EXPERIENCED TEAM CHALLENGES IN 2004

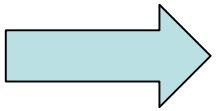
- **Global challenge: Create the first Integrative Systems Biology company based on a disruptive *"negative selection process"*,**
- **A concept contrary to "dominant" thinking.**

### Two main proofs of concept to succeed:

- **Scientific: Create the 1st *in-silico* model of a complex human disease to be validated *in-vivo*;**

- **Business: Set up a 1st spin-off company created from an internal integrative systems biology program.**

**Global critical issue: *Where to set up our company?***



**5 countries short listed to set up a business:**
**1 - CAN, 2 - CH, 3 - UK, 4 - SG, 5 - Fr. *(not the favorite country)***

# BMSystems: A fully international Co. in Paris.

## 2004 - BMSystems' team decides to set up its Co. in France for 4 reasons:

- **Young Innovative Enterprise Status, and R&D tax credit**
- **Key academic scientific teams identified & willing to collaborate**
- **Creation of clusters of interest**
- ***And finally, France is a nice place to live in!***

## While taking advantage of its founders' international networks:

- **Scientific Committee of the Cambridge Healthtech Institute USA (2005-)**
- **Welcome Trust's Board of Experts, Systems Biology. U. K. (2001-)**
- **Human Genome Organization (HUGO); (USA) (1994-)**
- **Medical Research Council (MRC); U.K. (1989-)**
- **Max Planck Munich Germany (2006-)**
- **Medical Systems Biology- MedSys"ministry of Research; Berlin (2008-)**
- **Etc …**

# BMSystems: a collaborative biotech company focused on its core know-how to optimize time to market & R.O.I.

- **Independent Private Company incorporated in 2004.**
- **Young Innovative Enterprise status since creation.**
- ***100% owned by its founders*** **(no search for external investors)**
- **A "*Biology" driven company* that intensively uses I.T. resources.**
- **Inventor and exclusive owner of all its technologies.**
- **All non-strategic functions and resources are externalized.**
- **FTE*: 9 scientists/professionals only focused on CADI™ research.**
- **Over 100 professionals are working on BMSystems' related programs.**
- **Member of BiO (USA), MEDICEN, IAR (Industrial biotech) clusters.**
- **Controls 40% of its biopharmaceutical spin-off: Pherecydes-Pharma.**

Building CADI™ models and validating them/developing outputs do not require the same competences and resources.
We prefer to share costs and profits with complementary partners.

*FTE: Full time Equivalent

# The Life-modeling issue

If you dream to create the first operational bird model…

*… a "basic" living Complex system that not only flies…*

Be sure to use the appropriate modeling concepts & tools. If not…

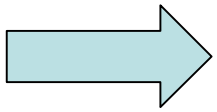
*…you get a Complicated "Cartesian" system. It does fly, but…*

**The challenge is clearly not a question of technologies only**

# The Life science modeling dilemma

1. The mechanisms of life are *complex, non-linear and integrative*
2. In "living complex" systems, the functions of *biological components and mechanisms are event and context-dependent*. The same components/networks can produce different biological effects
3. Classical "Cartesian" modeling concepts & approaches, valid for the majority of man-made artifacts, imply the concept of a "blue-print". Components are "function-specific" and their assembly pattern determines the final function of the structure they constitute. *But this concept is at the opposite of biological reality*
4. … While "Cartesian" Bioinformatics and *Mathematical tools have proven to be efficient to* collect, structure, analyze, simulate specific functions to test or to generate innovative hypotheses, yet…
5. …The *"garbage in, garbage out" reality*, tells us that the information produced and published (even in leading scientific journals) is necessarily *ALWAYS incomplete, biased and erroneous to unknown extents*

**Despite increasing investments in Technology &I.T., major drugs products submissions to FDA are constantly declining**

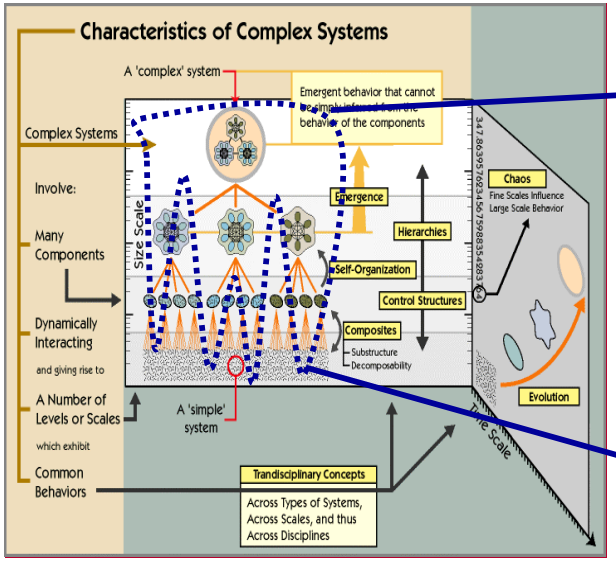


We need to change our point of view

# We invented CADI*™ "non-mathematical" modeling, successfully applying its 5 principles

1. An *"Architectural Principles"* Approach
2. Our *"Negative Selection"* Process
3. Our *"4 steps validation"* Process
4. Our *"Broad life sciences & IT"* Expertise
5. Our "*synergic collaboration*" with classical IT partners

A complex system to study

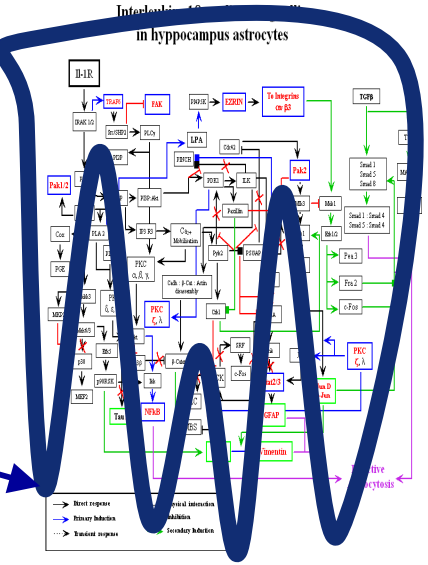



A CADI™ model representing the system in a specific context

Organs level

Cells level

Molecules level

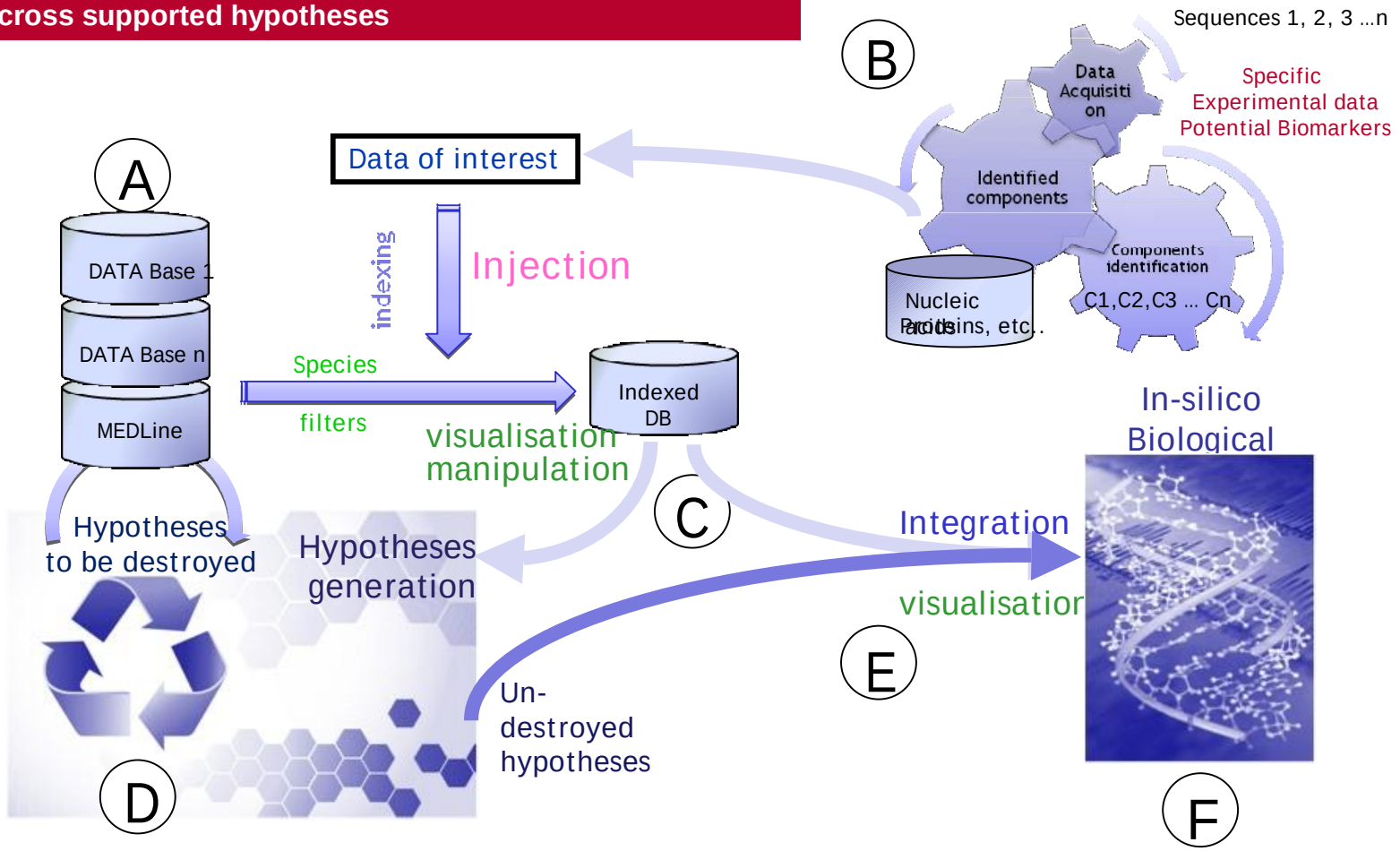



**Computer Assisted Deductive Integration*

# CADI™ negative selection process

The first operational application of the negative selection concept

**CADI™ original concept is an operative answer to "the garbage in garbage out issue", and a disruptive innovative way to generate new knowledge from new cross supported hypotheses**



# *Synergic collaboration* with classical IT partners

The first operational application of the negative selection concept

Let's go a step beyond with partners.
The pharmaceutical industry now requires its *scientists and clinicians* to harness & explain the mechanisms of health and diseases.

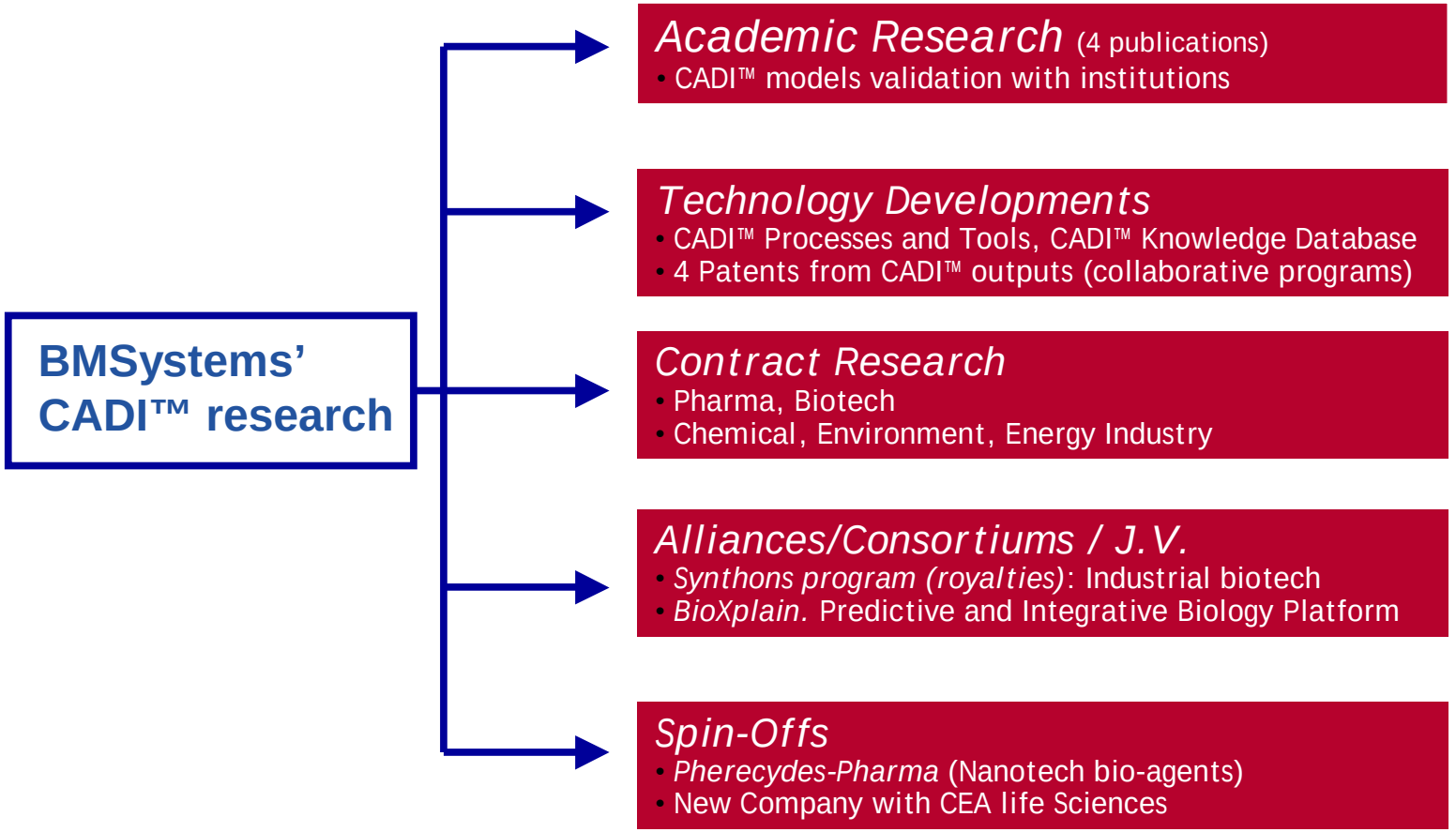
But they need *adapted systems and tools to help them work.*

Three complementary, cutting edge life sciences companies decided to collaborate to address this challenge:

- *Bio-Modeling Systems*: The inventor of CADI™ methodologies and tools, including the collaborative iterative validation process.
- *BioXpr:* The most diversified provider of Software solutions built from a versatile library of modules to create real-added value from "OMICS" datasets.
- *Kayentis:* The provider of the first "Digital Pen and Paper technology 2.0", the universal platform delivering "contextualized" information .

**BioXplain: The first Open Platform for Iterative Predictive and Integrative Systems Biology.**

# A collaborative strategy to optimize capital investments and time to market



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# BMSystems' CADI™ programs to date

| Program Name | Validation / Business Partner(s) | Feasib. study | CADI™ vers. 0 | Ind. Valid. | Patents / Publi. | First Proof of Concept (POC) | Mid scale or preclinic. P.O.C. | Ready for Business |
|---|---|---|---|---|---|---|---|---|
| Nano-Bioagents | Pherecydes | | | | | | | |
| TAPE | Pherecydes | | | | | | | |
| Chronic Fatigue Syndrome | Open | | | | | | | |
| Ebola virus ecology | Open | | | | | | | |
| Hepatitis C | Open | | | | | | | |
| CNS-Psychiatry | CEA Life Sciences | | | | | | | |
| CNS-Neurodegenerative | CEA Life Sciences | | | | | | | |
| Fibromyalgia | Open | | | | | | | |
| Pain | Open | | | | | | | |
| Migraine | Open | | | | | | | |
| Multiple Sclerosis | Open | | | | | | | |
| Psychiatric disorders | Open | | | | | | | |
| Program Synthons | ARD-IBT-L'Oréal | | | | | | | |
| Program Synthons | ARD-IBT-Rhodia | | | | | | | |
| Program Synthons | ARD-IBT-Arkema | | | | | | | |
| Breast cancer-Hras | INSERM | | | | | | | |
| Tamoxifen resistance | INSERM | | | | | | | |
| Metastasis mechanism | INSERM | | | | | | | |
| Müllerian regression | CNRS | | | | | | | |
| Adipocytes growth control | Open | | | | | | | |
| Hypercholestemia | Open | | | | | | | |
| Metabolic Syndrome | Open | | | | | | | |

# Synthons program, major collaborative industrial biotech research platform in the IAR world-class cluster

## A complementary collaborative team:

- **A.R.D.: Leading Industrial Biotech research company with experimental capacities, pilot scale-up, pilot plant (2000 Tons), etc.**
- **I.B.T.: One of France's leading Technology Transfer Institutes.**
- **BMSystems: integrative Biology & metabolic engineering expertise.**
- **C.V.G.:"green chemical" sourcing research institute.**

## 3 EU chemical companies proposing their molecules to the platform:

- **L'Oréal: (world leader in cosmetics)**
- **Rhodia: (ex Sanofi Aventis fine chemical entity)**
- **Arkema: (ex Total chemical entity)**

2 engineered strains generated are under evaluation and a finalized process under mid-scale validation. The program is funded by the ministry of Industry and supported by IAR world-class cluster

# The double take win-win collaborative programs

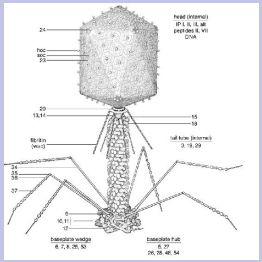
1. **2008: *World's first in-vivo validation of a CADI™ in-silico model* of a complex human disease (Creutzfeldt-Jakob/prion disease) with CEA SEPIA*, coordinator of the European NeuroPrion Network of Excellence. Discovery of a new regulation system in the brain. (publi. Pending)**

→ **The program received a prestigious US Industry Award:**
**Bio-IT World 2009 Best Practice Award**
**The only EU team rewarded in 2009**


2. **2009: *New industrial application*: A 2nd CADI™ model with the same research team, exploiting one discovery of the 1st CADI™ model, led to the discovery of novel therapeutic approaches in the treatment of poorly served psychiatric diseases (patent filed Sept 2008).**

→ **In 2009, BMSystems and CEA Life Sciences decided to support a spin-off research team to develop the patent.**

*CEA (Atomic Research Council) Department of prion and atypical infections research (SEPIA) **A department of the CEA IMETI Institute**. **Jean-Philippe Deslys, Franck Mouthon and Pierre Chagvardieff.**



# PHERECYDES-PHARMA: Less that 5 years from concept to industrial proof in the field of biodefense /biosecurity.

- *World's 1st company created from an integrative systems biology program*
- **Creation of the *first operational large-scale engineered bacteriophage bank* to fight against *"unknown multi-resistant" bacterial infections*.**
- ***Outstanding support from CEA Fontenay-aux Roses* (founding member of Medicen cluster), including IMETI* Institute's scientific team.**
- **Creation Dec. 2006: *1.15 Million € raised*, from ACE management funds.**
- ***500 k € Innovation Program grant* from Oséo Innovation Agency.**
- **Rapid international recognition in the USA *(4 invitations to present*).**
- ***3 fully owned international patents* invented by BMSystems.**
- ***Industrial proof of concept:* Sept. 2009.**
- **April 2010: signs its *first international collaboration with BAC (Bio Affinity Company) BV* to develop improved antibodies and is negotiating 2 others in N. America.**
- **Pherecydes Pharma is member of Medicen and is also supported by the Lyon Biopôle cluster.**

**Clearly, the outstanding collaboration & support from CEA life Sciences Fontenay-aux-Roses, led to Pherecydes-Pharma being located in France**

*Pr. Leboulch, Jean-Philippe Deslys, Franck Mouthon and Pierre Chagvardieff

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# Clients & Partners of BioXplain founders
## Diversified complementary network

# Conclusions / Questions

**For more information:**

- www.bmsystems.net
- www.pherecydes-pharma.com
- Email: manuel.gea@bmsystems.net

**To meet us during BiO:**

- Booth 3712 UBI FRANCE-MEDICEN
- BiO Partnering Forum