Is Life Science the New Frontier of Design Automation?

A 45 year perspective on DA

Alberto Sangiovanni-Vincentelli

The Edgar L. and Harold H. Buttner Chair of EECS
University of California, Berkeley

Co-founder and Member of the Board,
Cadence Design Systems

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Market Summary > Cadence Design Systems Inc

203.52 USD

NASDAQ: CDNS

+164.93 (427.39%) ↑ past 5 years

Closed: Mar 14, 4:45 PM EDT • Disclaimer

After hours 203.98 +0.46 (0.23%)

1D | 5D | 1M | 6M | YTD | 1Y | 5Y | Max

Open	197.86	Mkt cap	55.55B	52-wk high	203.68
High	203.68	P/E ratio	65.93	52-wk low	132.32
Low	197.42	Div yield	-		

Cadence Design Systems Inc

NASDAQ: CDNS

cadence.com

Cadence Design Systems, Inc., headquartered in San Jose, California, is an American multinational computational software company, founded in 1988 by the merger of SDA Systems and ECAD, Inc. Wikipedia

CEO: Anirudh Devgan (Dec 15, 2021–)

Founded: 1988

Headquarters: San Jose, CA

Number of employees: 10,200 (2022)

Revenue: 3.56 billion USD (2022)

Founders: Alberto Sangiovanni-Vincentelli, A. Richard Newton

Subsidiaries: Tensilica, Sigrity, OpenEye Scientific Software, MORE

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Agenda

- How did we go from handcrafted designs to a scientific process in EDA?
- The Birth of EDA as we know it today
- The future of classical EDA
- System Level Design
- Back to the Future: Life Sciences and EDA

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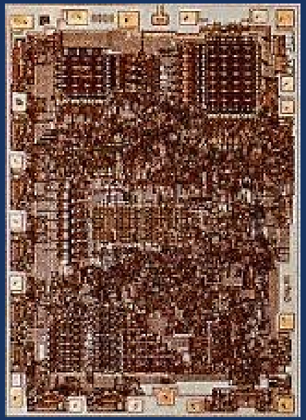
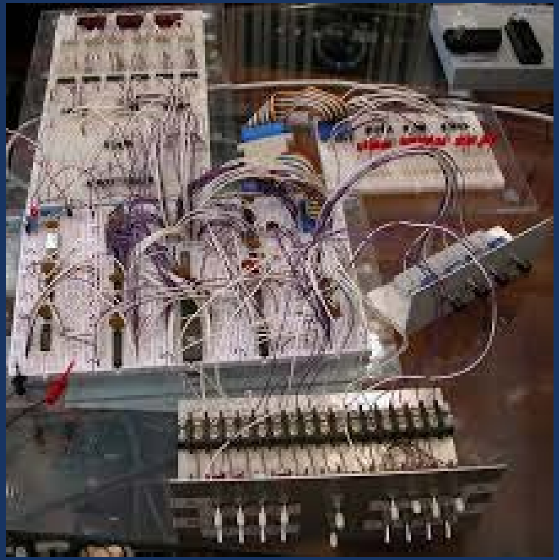
Once upon a Time… 1971 (when I graduated)

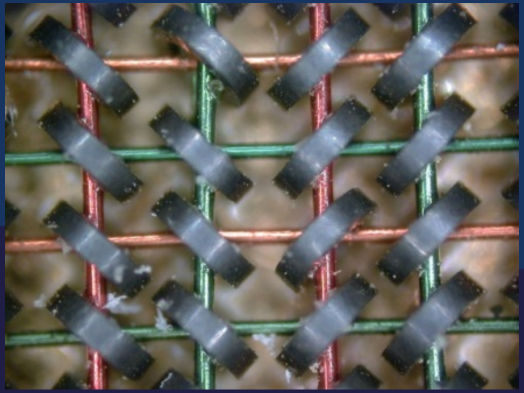


3,500 Transistors, 92K IPS

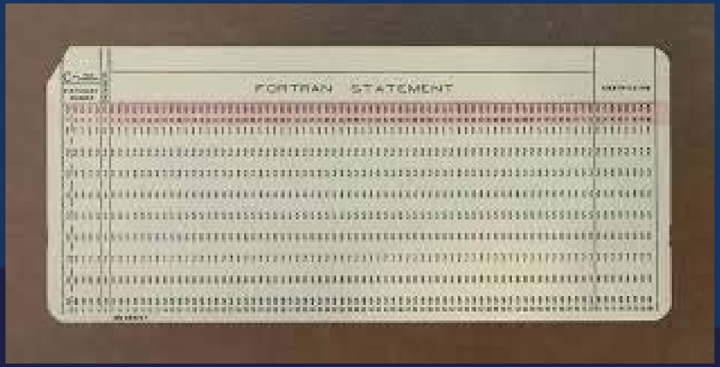


Verifying the chip

Preparing the masks



Magnetic-core memories



Punched card

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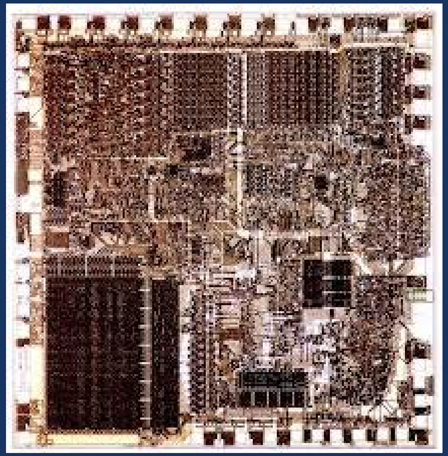
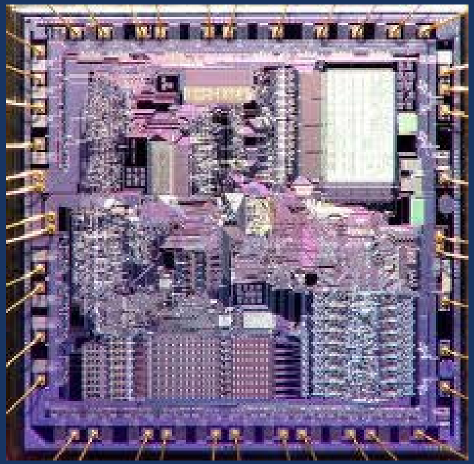
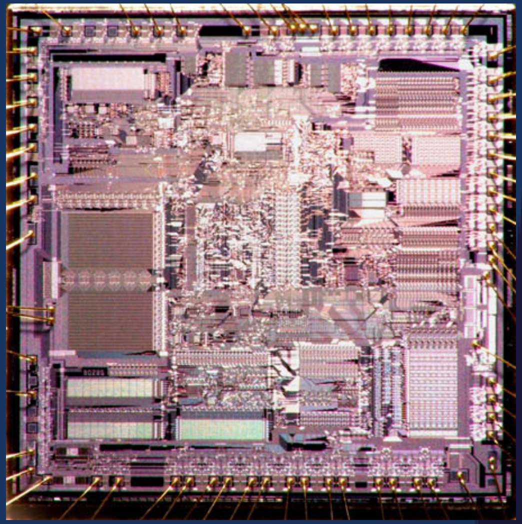
Evolution: From Handcraft to...



Intel 4004



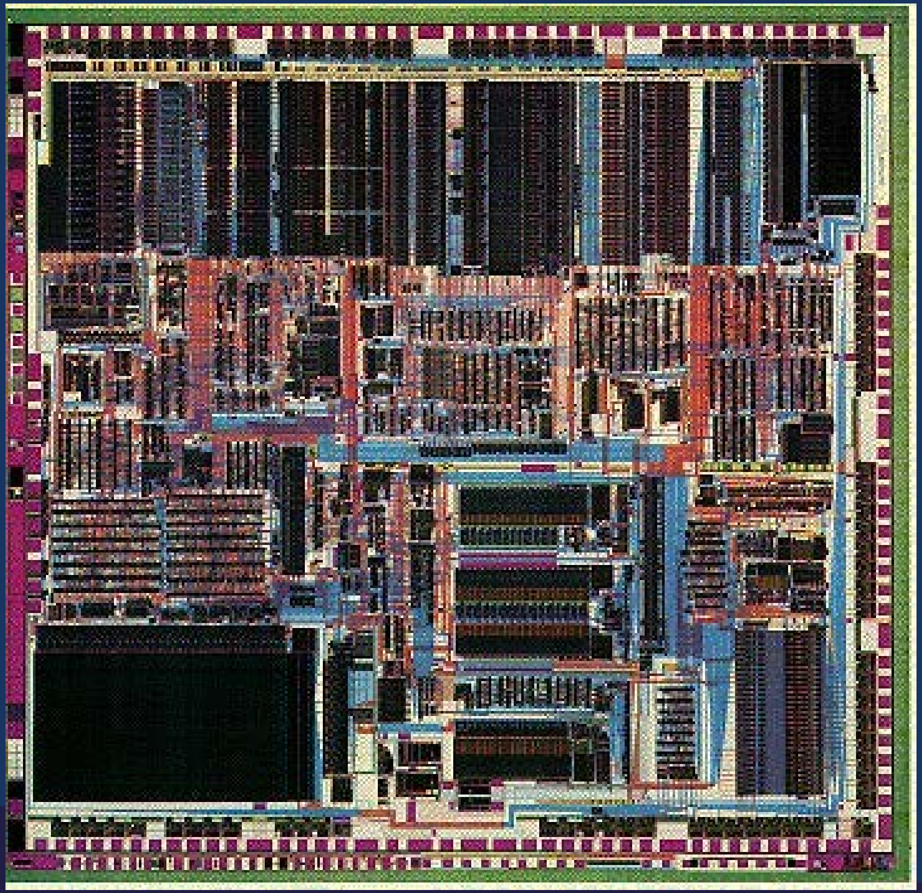
Intel 8086



Intel 80286

To… Methodology:

Logic Abstraction, Regularity, Libraries, and Tools!



Intel 386

1983, Intel 386
275,000 Transistors

Industry complexity problems spurred theoretical research that ended up in at least 80 papers, DARPA grants , awards, and

start-ups

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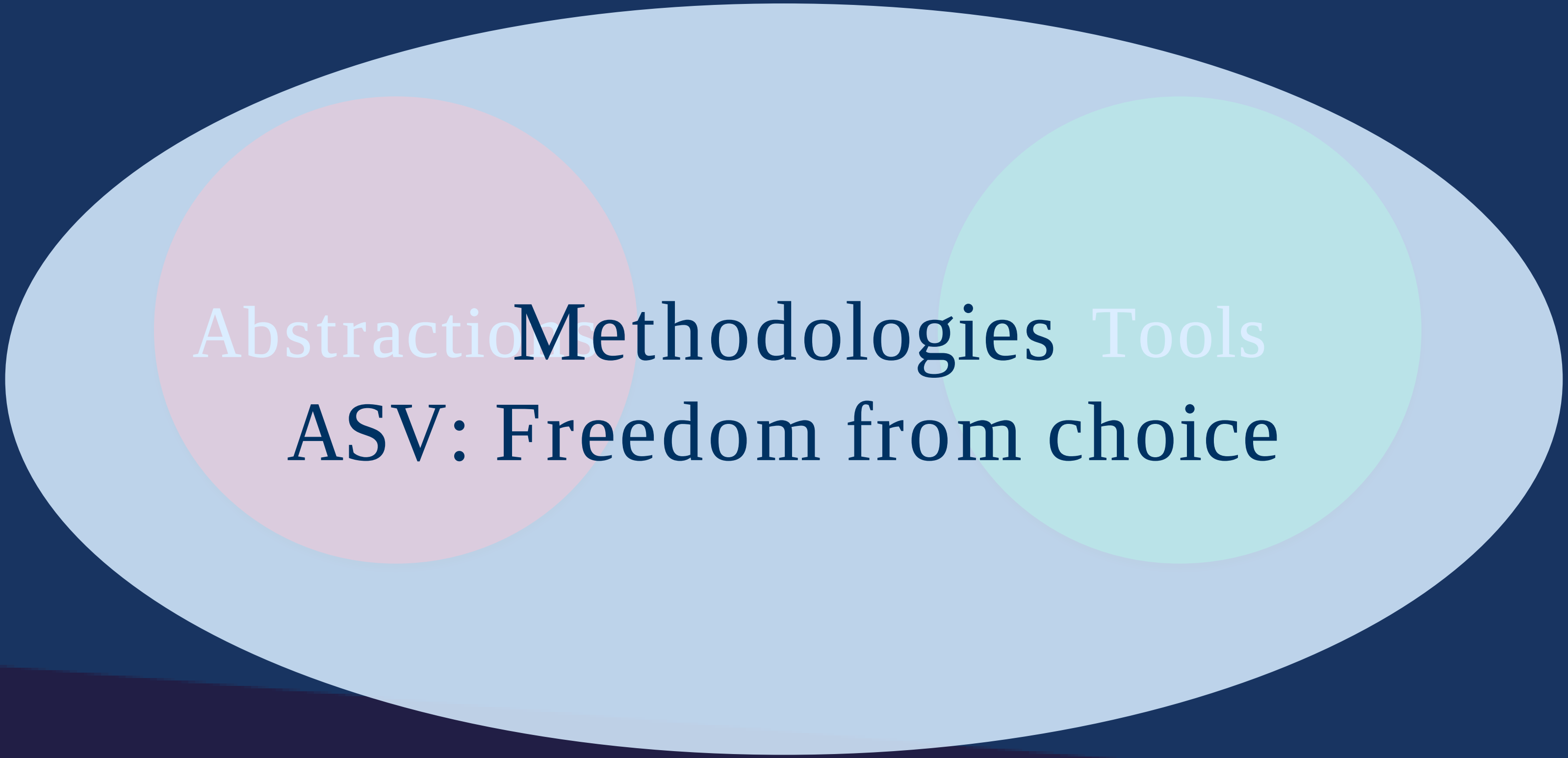
How Did We Cope with Complexity?

ASV, Corsi e Ricorsi: The EDA Story, IEEE Solid State Circuits Magazine, 2010

A Live Person quote!



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Time to Offload the Ball!

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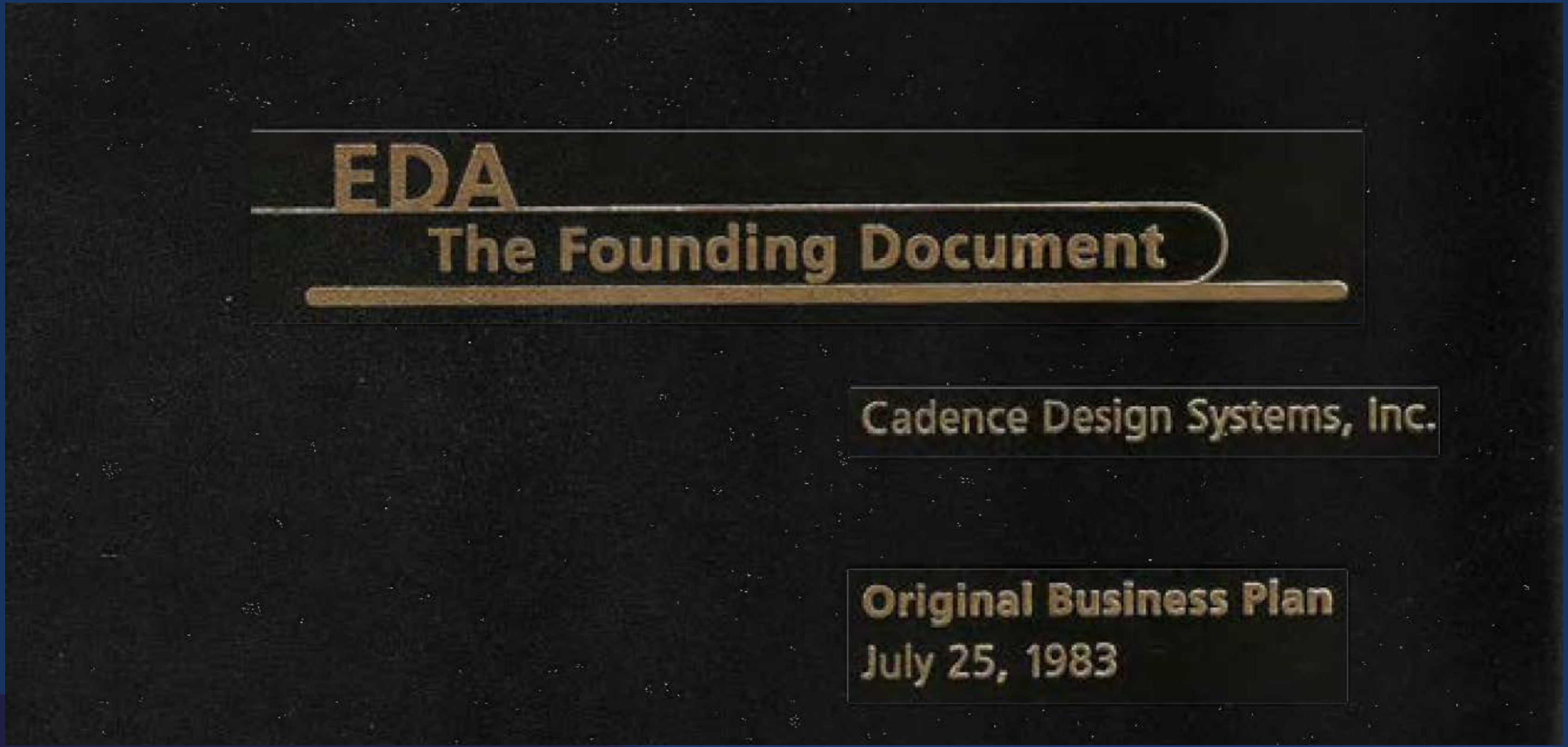
The Origin of Cadence



CONFIDENTIAL

BUSINESS PLAN FOR:

ISIS SYSTEMS, INC.

A NEW CORPORATION IN ELECTRONIC DESIGN AUTOMATION

July 25, 1983

Copy No. S-7

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The Basic Tenets: a Complete Methodology

- Framework based on a unified database and graphical user interface
- FIRST software-only company based on Unix workstations,
- Full suite of physical verification (DRC, ERC) and simulation (circuit, logic and mixed)
- Automatic layout for macro cell, standard cell and gate array design styles
- New funding model: mixed VC (4M$) and companies (National, Harris, GE, Ericsson) (6M$)
- Public in 1988

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Synopsys:

- Funded in 1987 (DeGeus, Newton, ASV)
- Based on automatic synthesis
- Same funding model as Cadence: VCs and companies (GE, Harris)
- Public in 1991

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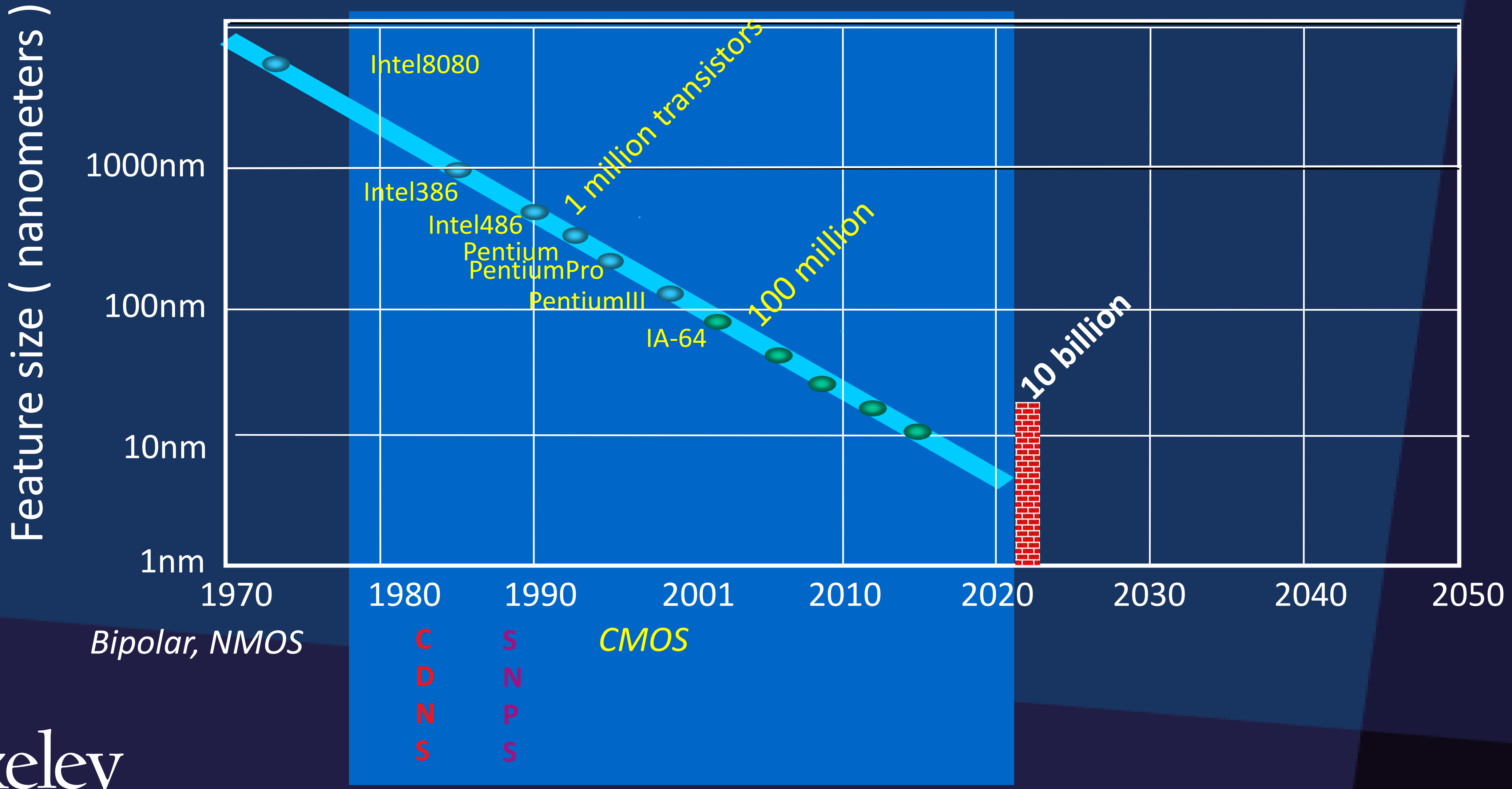
Coping with Moore's Law: The Role of Cadence and Synopsys



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Palafitte
2010

DESIGN “PRACTICE”

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Segesta (Σέγεστα) Temple, Sicily, 420 BC
(Picture Taken 2020)

DESIGN SCIENCE:
Principles not Techniques

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General Principles

- **Verification complexity is managed by:**
  - **Abstraction**: Reduce the number of items by aggregating objects and by eliminating unnecessary details with respect to the goal at hand
  - **Decomposition**: Reduce the number of items to consider by breaking the design object into semi-independent parts (divide et impera)

- **Design complexity is managed by "construction":**
  - **Refinement**: Start high in the abstraction layers and define a number of refinement steps that go from the initial description to the final implementation
  - **Composition**: Assemble designs by composing existing parts

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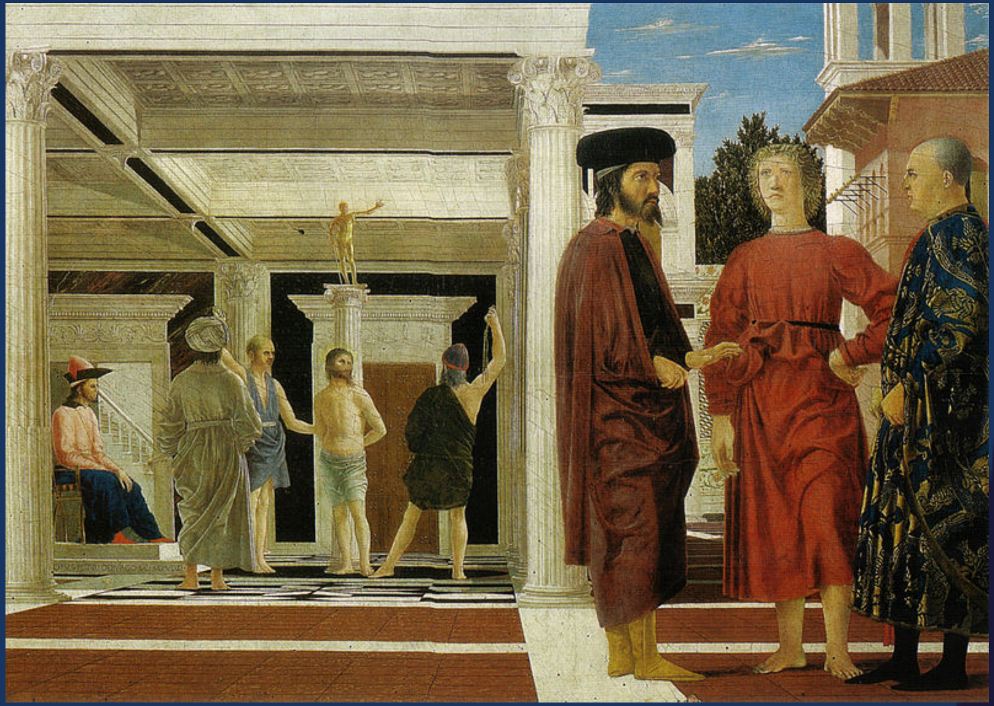
Formalization



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Virtual Design and Refinement

Library-based Design Reuse

Plug and Pray!

Courtesy of Edward Lee

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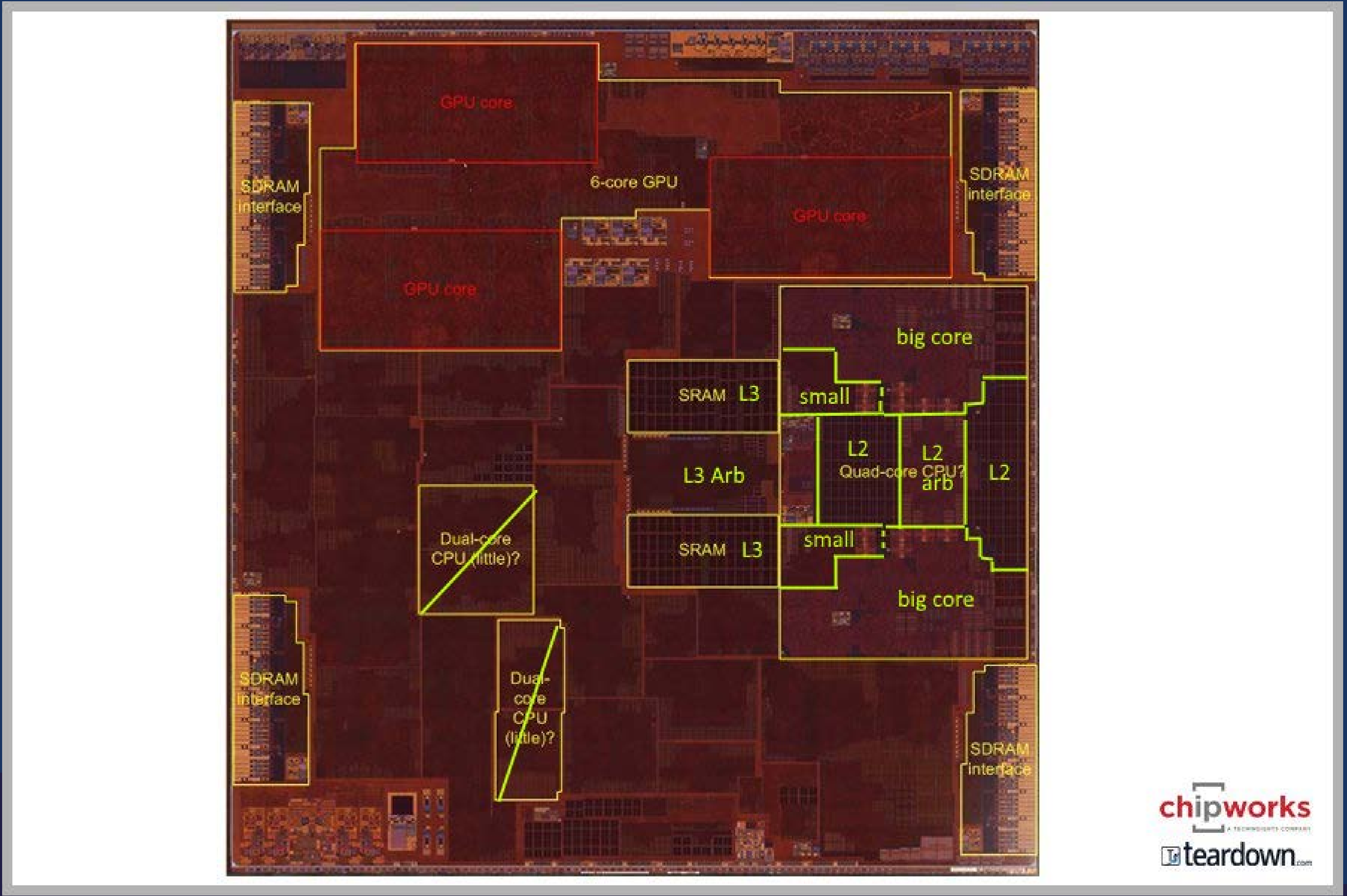
Today's Monster Chips: Apple A11 4.3Billion transistors



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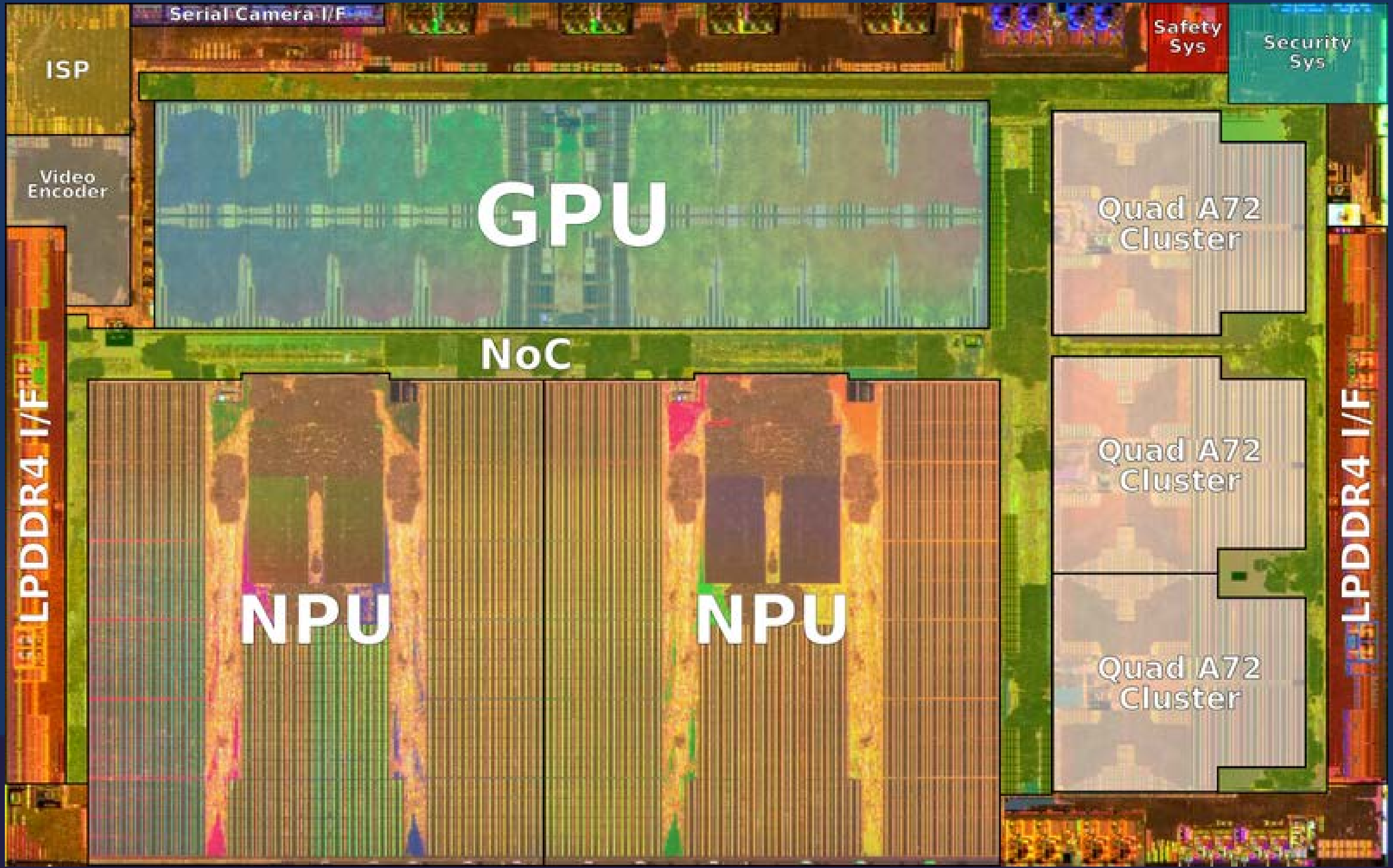
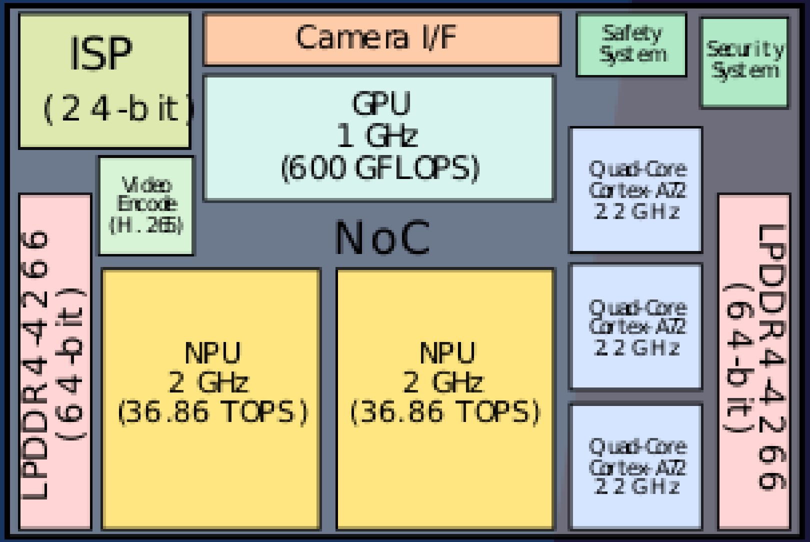
TESLA FSD SoC





NoC – Network on chip
ISP – Image Signal processing
Safety Sys – Lock step for ISO26262
Security – only TESLA certified software

Chip focused on Automotive L5 use case for Deep learning

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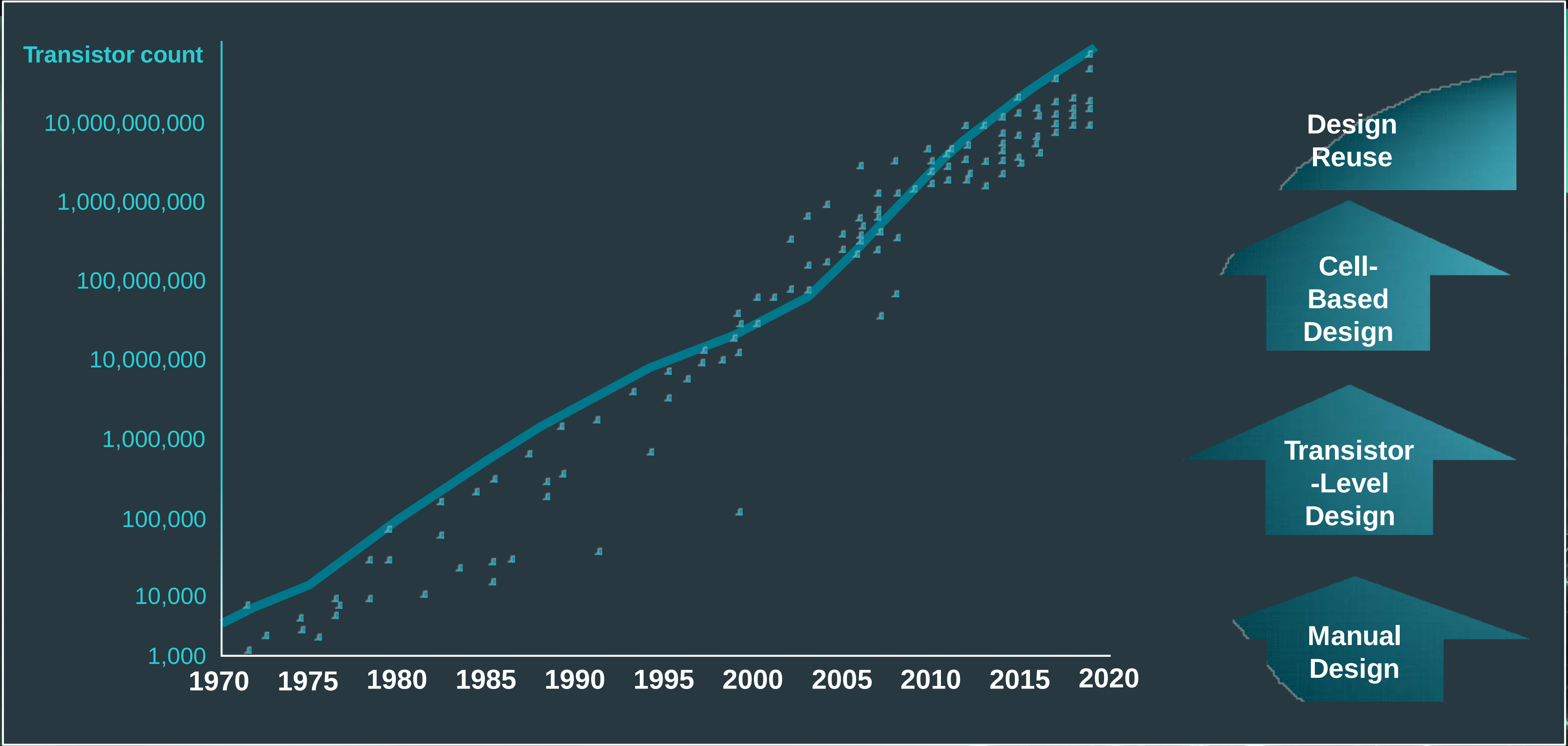
Summary: EDA Design Methodology



Source: Wikipedia (Wikipedia.org/wiki/Transistor_count)

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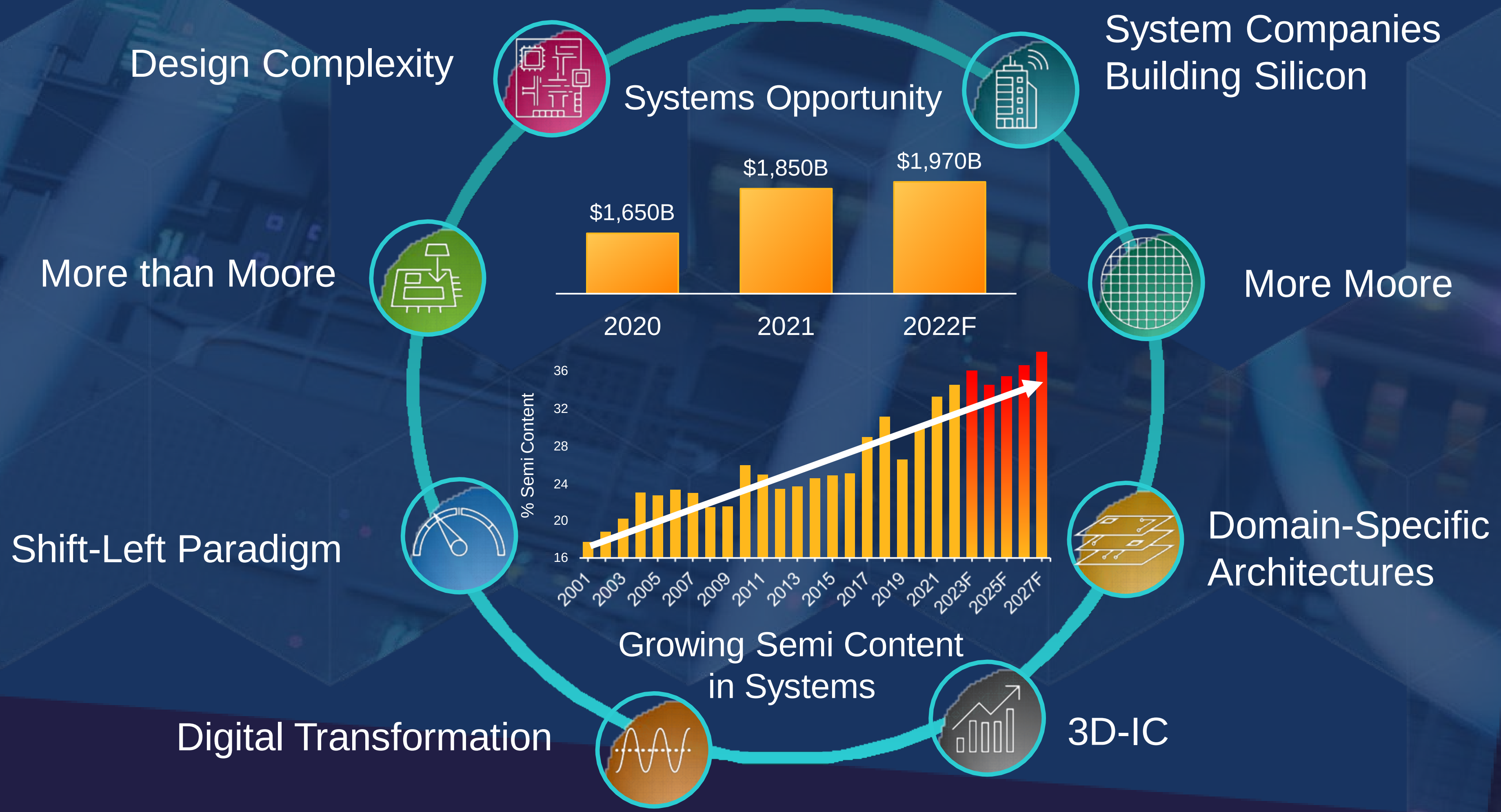
Long-Term Trends



Source: The McClean Report 2022, January Semiconductor Industry Flash Report, IC Insights, Inc.

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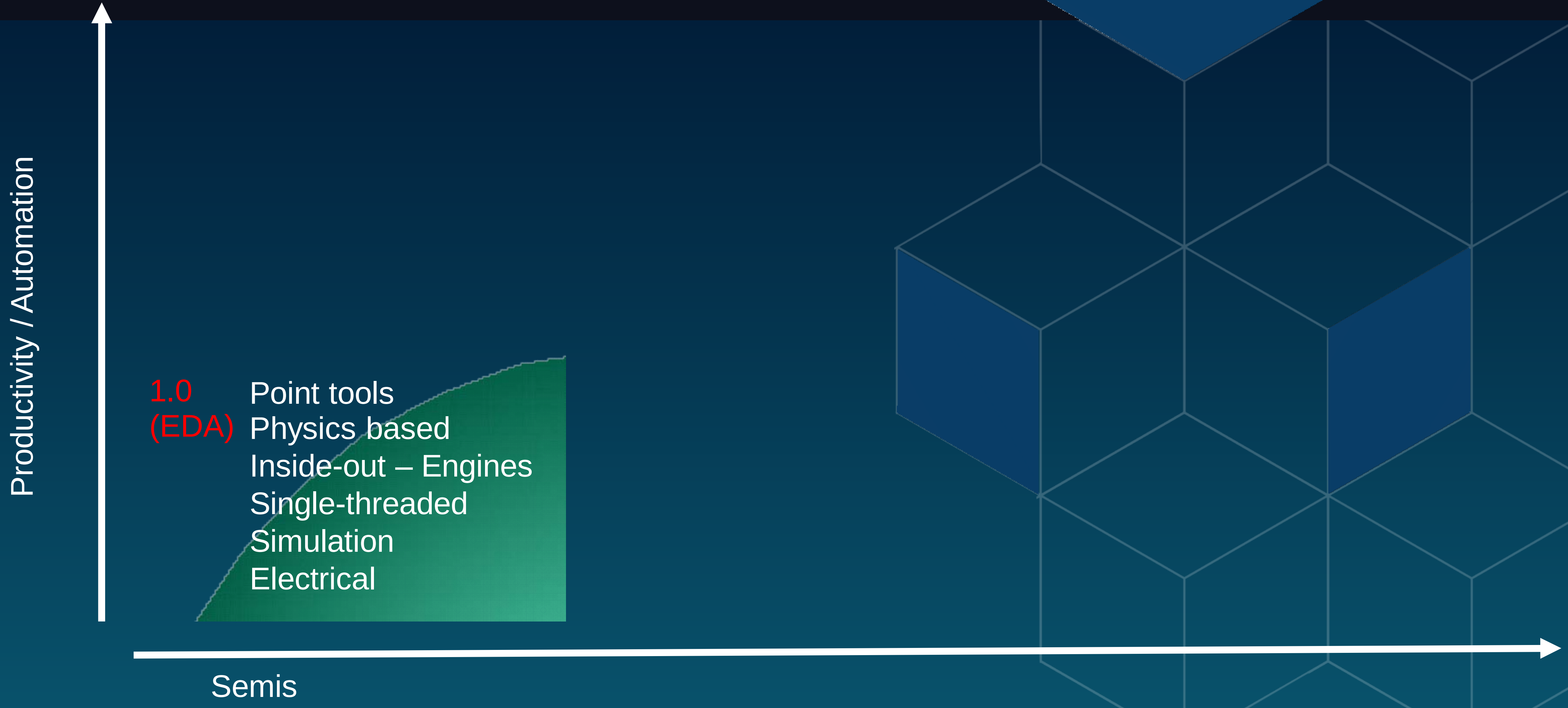
Computational Software – Transformational Impact



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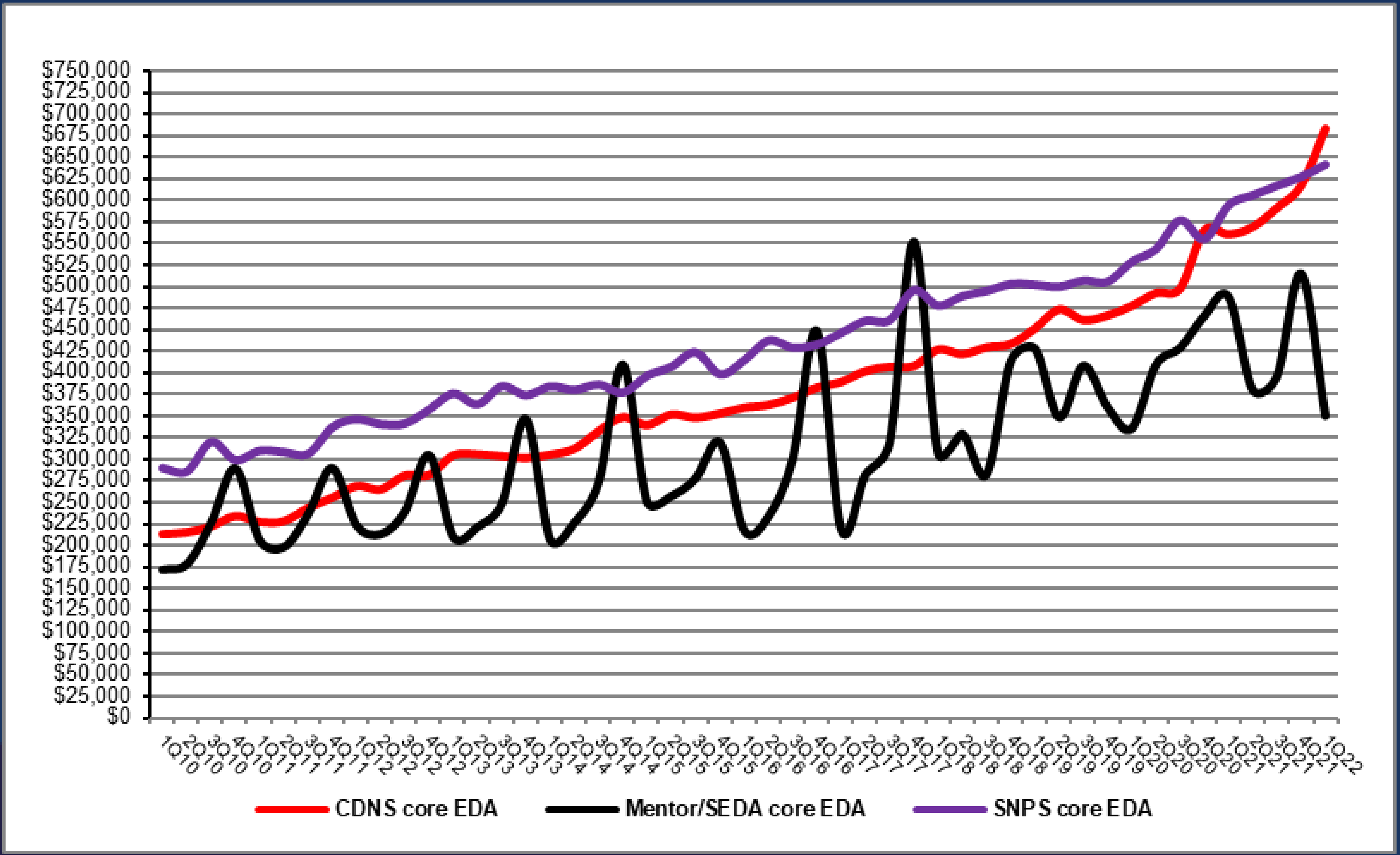
How are we doing now in core EDA?



Courtesy: Jay Vleeschhouwer
Software Research
Griffin Securities

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Broad Range of Secular Megatrends Driving Growth

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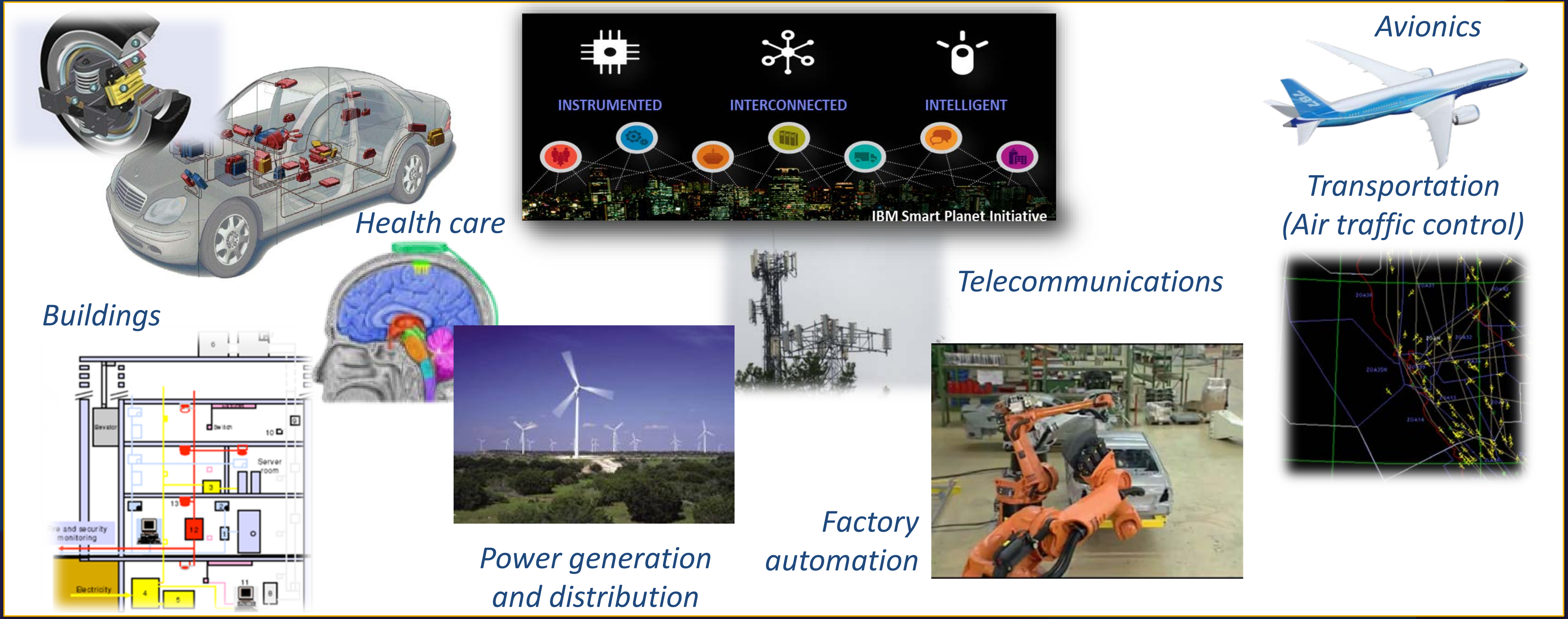
After Semiconductors? (1988)

Semi-automatic transmissions with paddle shift operation were first introduced to control the electro-hydraulic gear shift mechanism of the Ferrari 640 Formula One car in 1989.

Cyber-Physical Systems (CPS):

Interconnect the World Around Us and Make It "Smarter"



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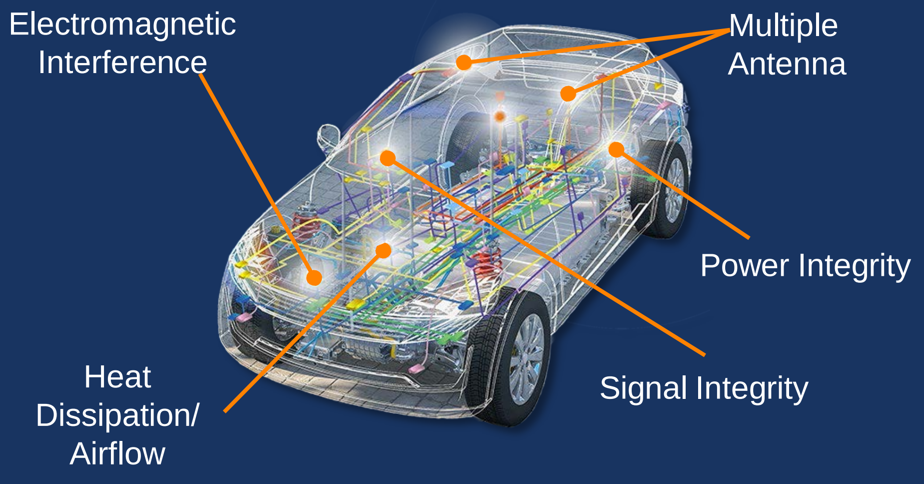
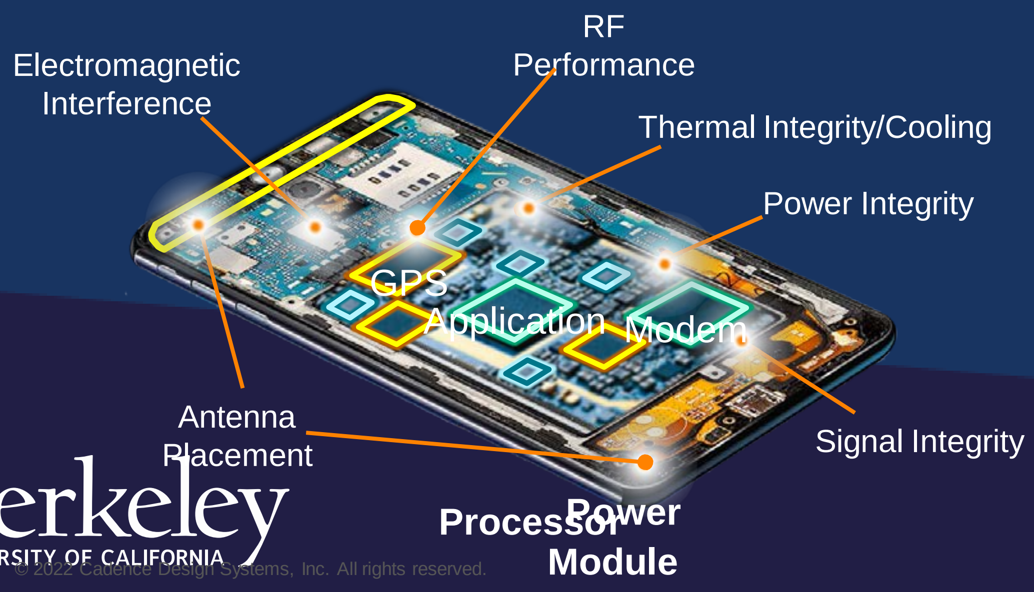
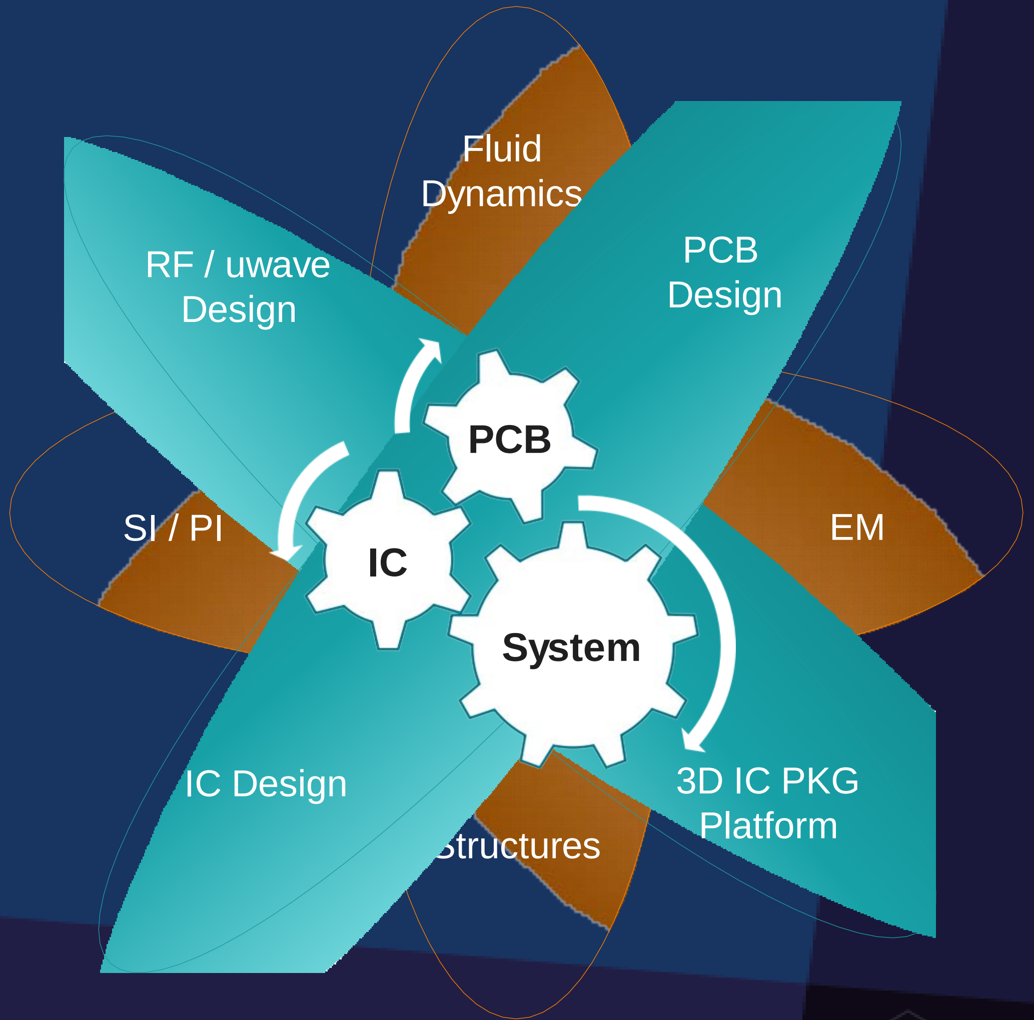
Integrated System Design and Analysis

Electronic / mechatronic system complexity exponentially increasing







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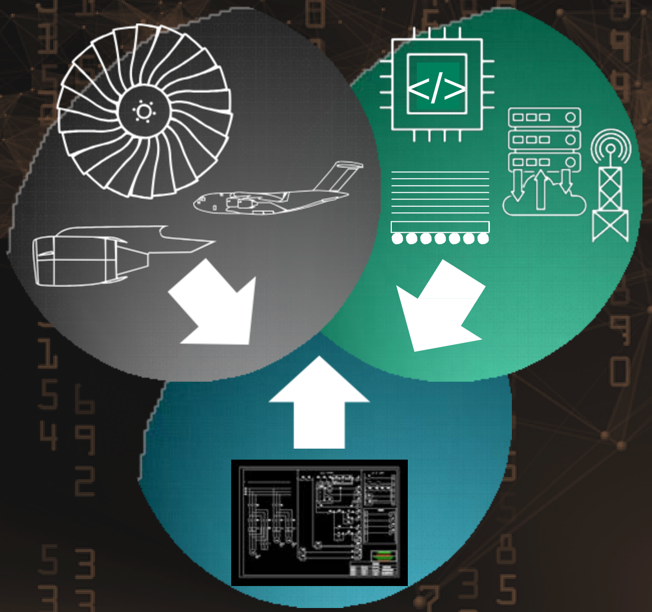
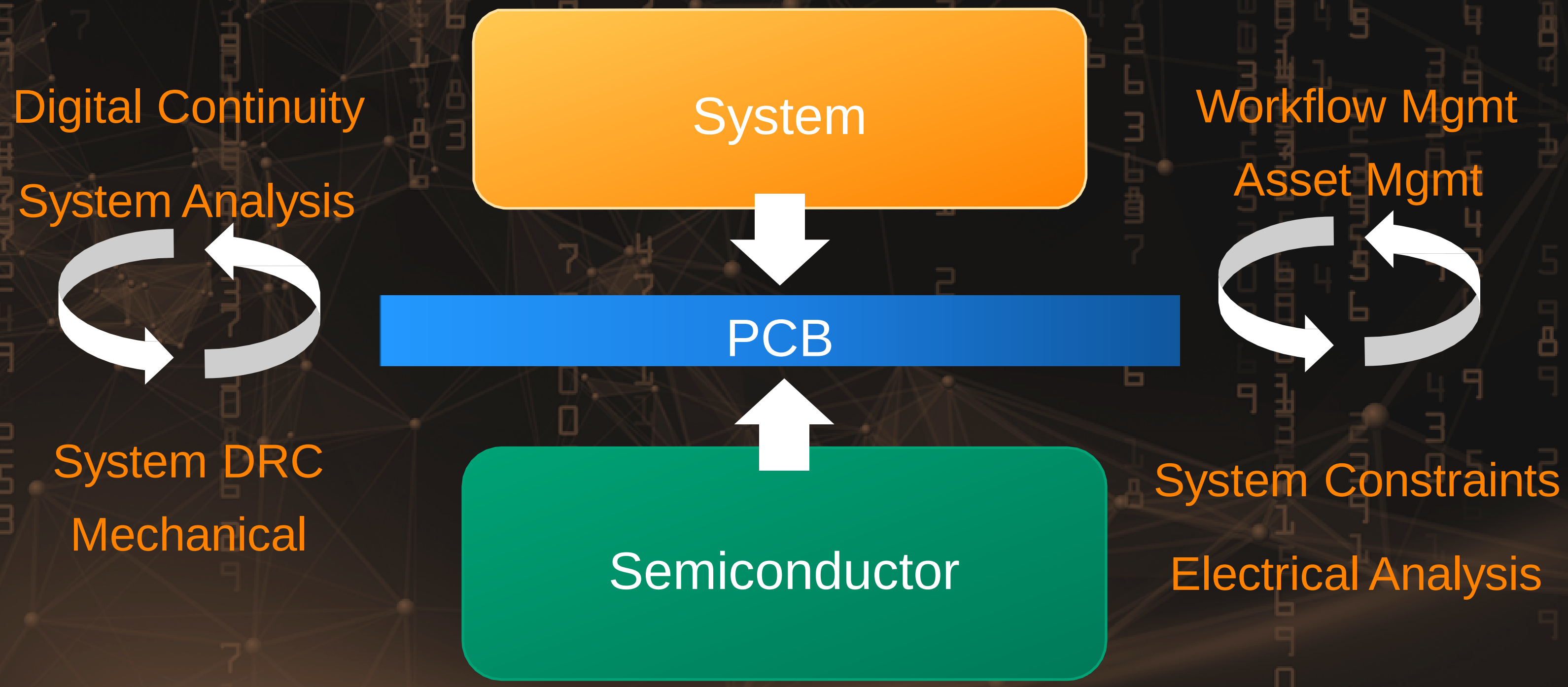
Accelerating Hyperconvergence => Faster System Realization

MECHANICAL

ANALYSIS



ELECTRICAL



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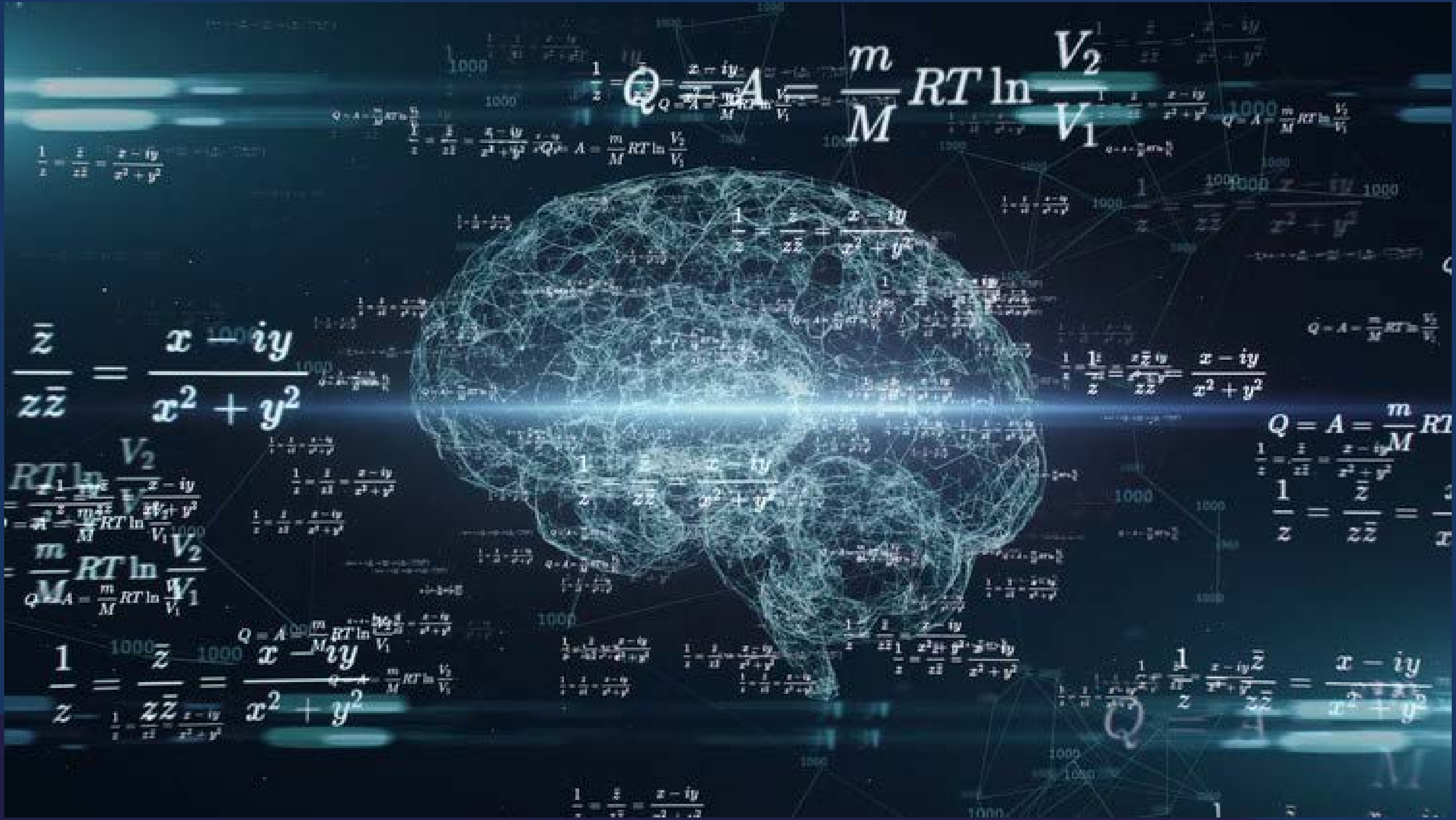
Computational Software… Is All About the Underlying Math



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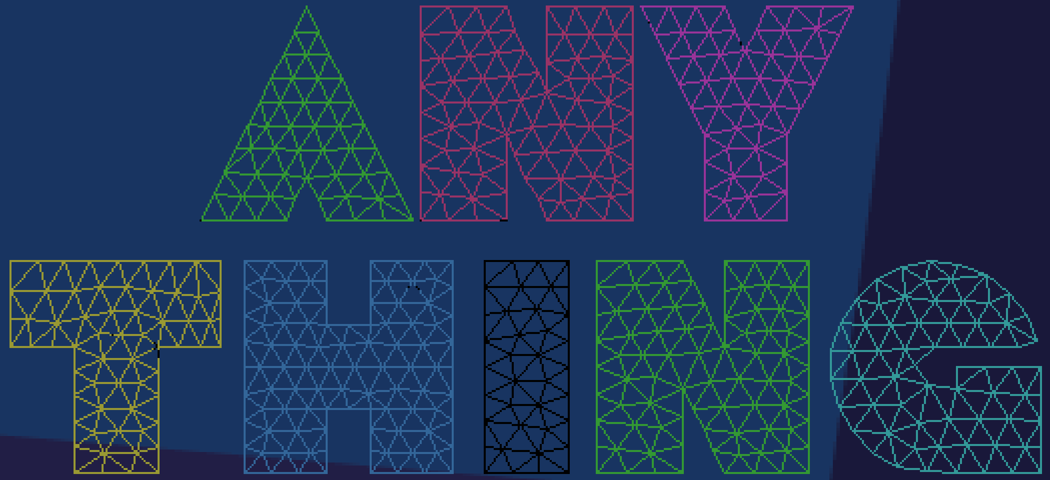
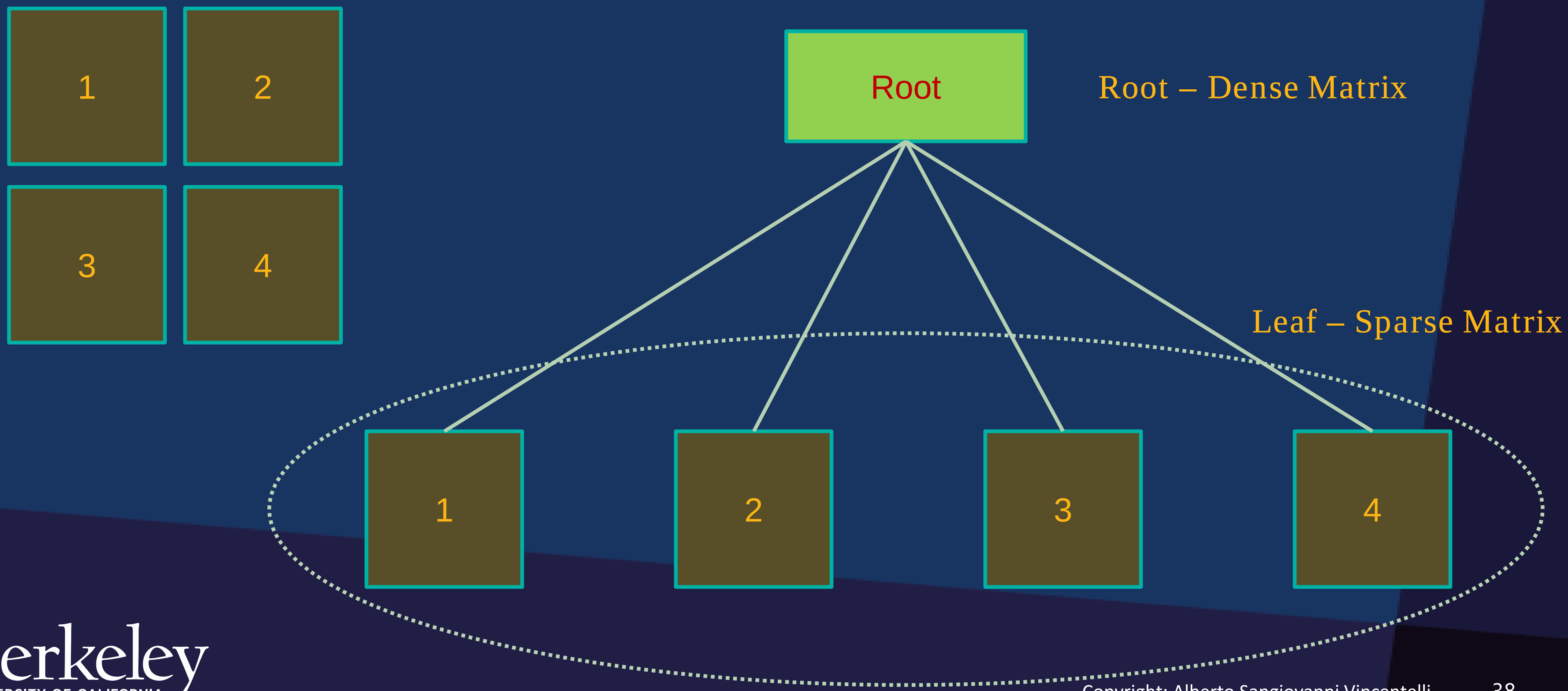
Finite Element Method

- The numerical method of choice to solve PDEs
- Discretize PDEs onto Meshes
- PDEs become linear sparse matrix to solve
- Performance/capacity of FEM solver is largely dependent on that of the sparse matrix solver

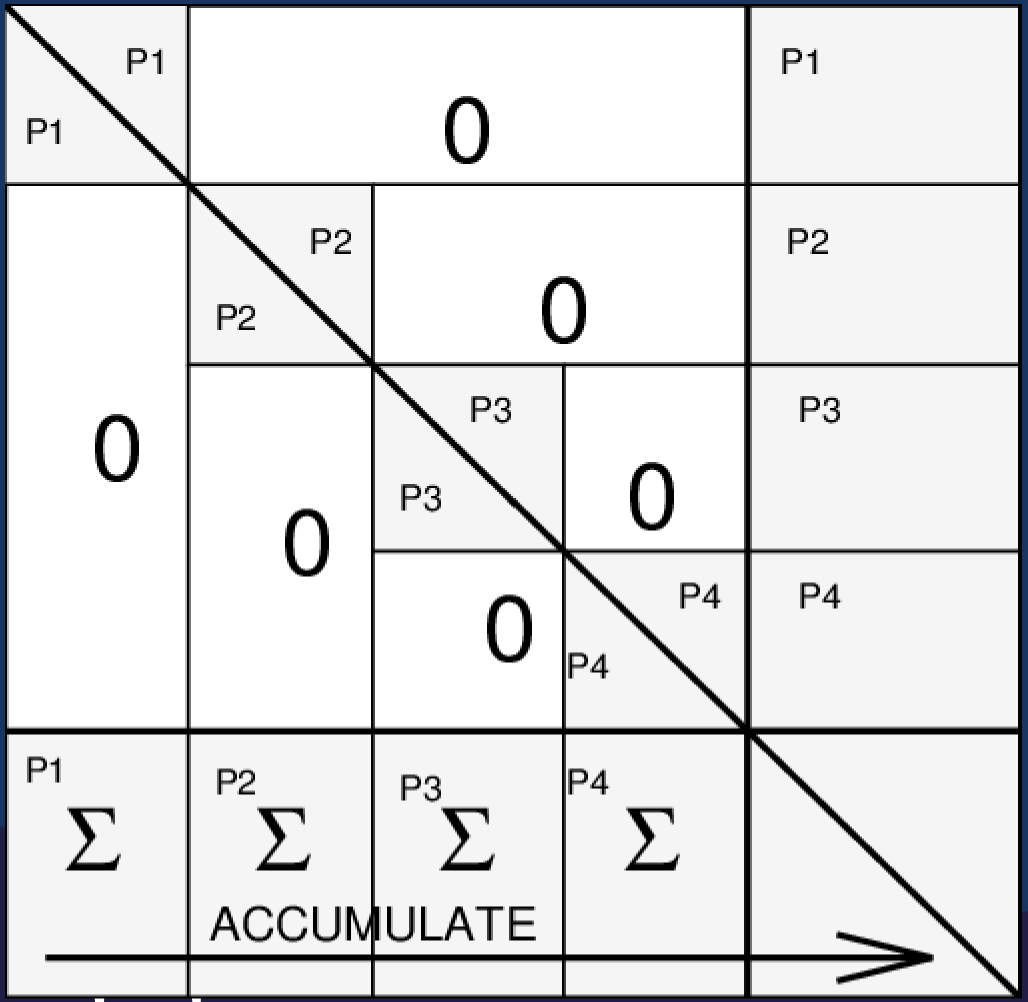


Distributed Matrix Solver



Distributed Matrix Solver

Takes advantage of structure of FEM



- Performance/capacity of solver heavily depends on quality of partitioning
- Leaf is sparse and Schur complement is dense

G. Guardabassi and A. Sangiovanni-Vincentelli
A two levels algorithm for tearing,
IEEE Transactions on Circuits and Systems 23 (12), 783-791, 1976

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Cadence M&A (Since 2019)

Company	Domain
Future Facilities	Datacenter Digital Twin
Pointwise	CFD meshing
NUMECA	CFD Solutions

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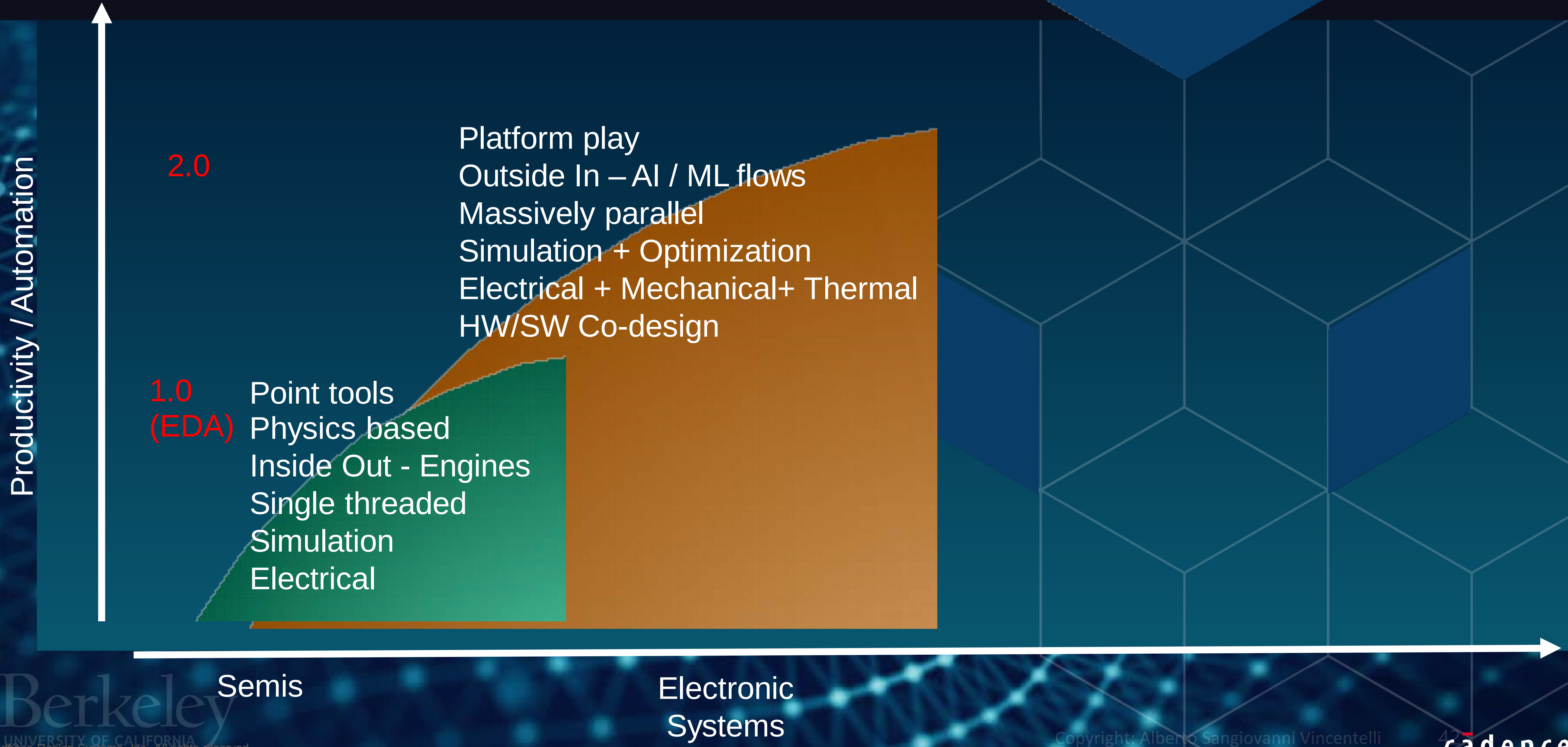
Computational Software – Transforming the Future



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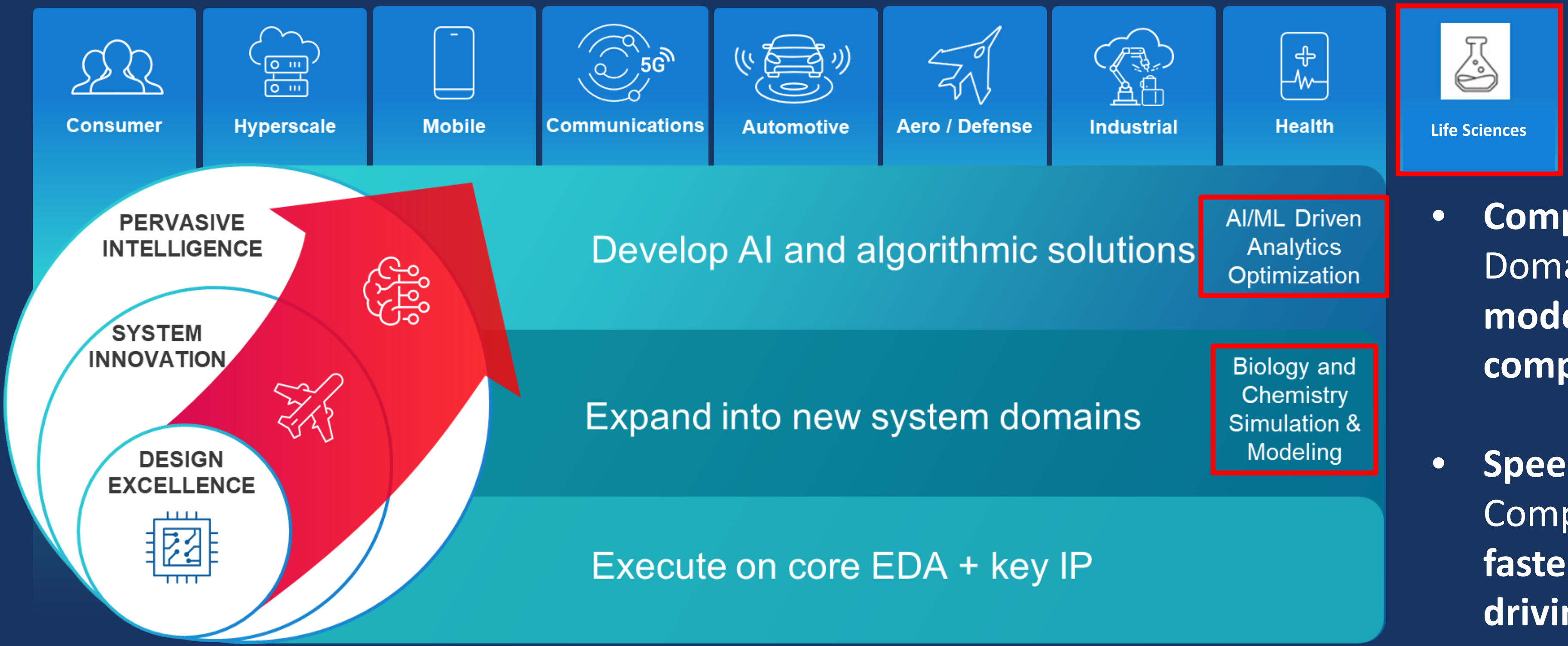
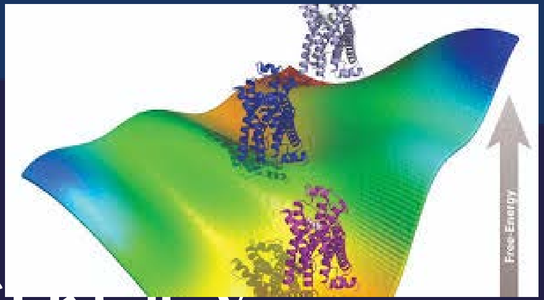
Cadence Intelligent System Design

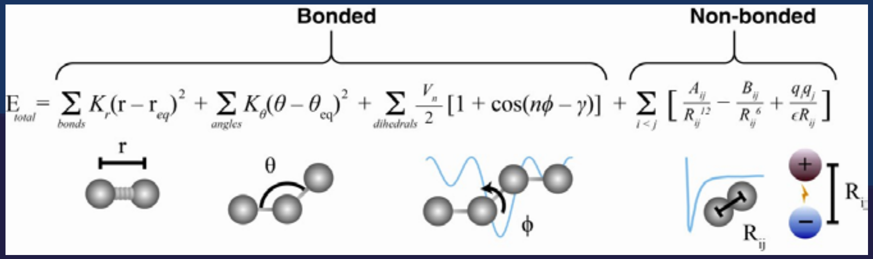
*Computational Software as a Core Competency → Expansion into **Computational Biology***



- **Computational Biology** is a System Domain with **complex physics, modeling and simulation → All core competencies of Cadence**
- **Speed Matters**; Cadence Computational methods can drive **faster, more complex, simulation → driving industry growth**
- **AI and Data Driven Drug Discovery/Design** are expanding fields



Molecular Dynamics Simulations



$$E_{total} = \sum_{bonds} K_r(r - r_{eq})^2 + \sum_{angles} K_\theta(\theta - \theta_{eq})^2 + \sum_{dihedrals} \frac{V_n}{2}[1 + \cos(n\phi - \gamma)] + \sum_{i<j} \left[\frac{A_{ij}}{R_{ij}^{12}} - \frac{B_{ij}}{R_{ij}^{6}} + \frac{q_i q_j}{\epsilon R_{ij}} \right]$$

Physics-based Modeling

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EDA and Biology: Personal Fascination

- Vertex Pharmaceuticals was one of the first biotech firms to use an explicit strategy of rational drug design rather than combinatorial chemistry. Greylock was one of the VCs who invested in Vertex.

- 1989 BioCAD, a biotech software company that was the first to apply EDA principles to pharmaceutical discovery (Steve Teig, exiting Cadence after Tangent acquisition)

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EDA and Biology: Personal Fascination

- Cadence Research Laboratories established in 1993 in Berkeley to focus on advanced research in electronic design automation, had a research project on Computational Biology
- Maria Di Benedetto, P. Lucibello, Alberto Sangiovanni-Vincentelli, and Ken Yamaguchi, Chain Closure: A Problem in Molecular CAD, *Proceedings of the 31th ACM/IEEE Design Automation Conference (DAC-94*), San Diego CA, pp. 497-502, Jun. 1994.
- Maria Di Benedetto, P. Lucibello, Alberto Sangiovanni-Vincentelli, and Ken Yamaguchi, New Procedure for Exact Ring Closure, *J. Computational Chemistry*, Vol. 21, No. 10, pp. 870-881, Jul. 2000.

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Platform-based Design Environment for Synthetic Biological Systems

Douglas Densmore (EECS, Boston University),
J.Christopher Anderson (Bioengineering),
Alberto Sangiovanni-Vincentelli (EECS)

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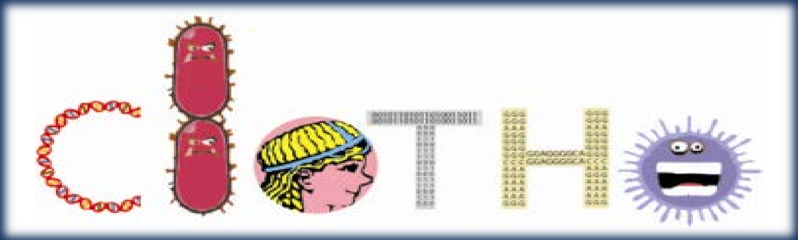
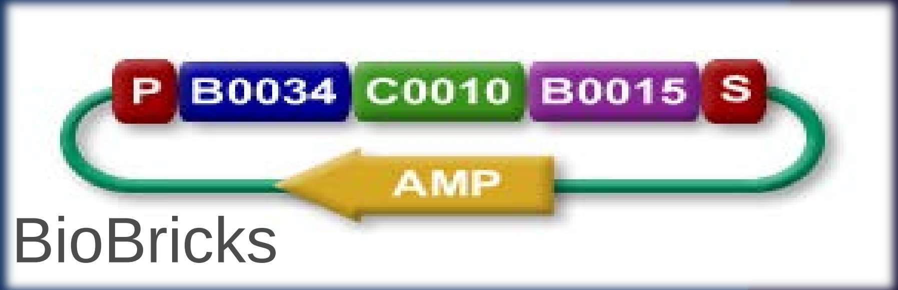
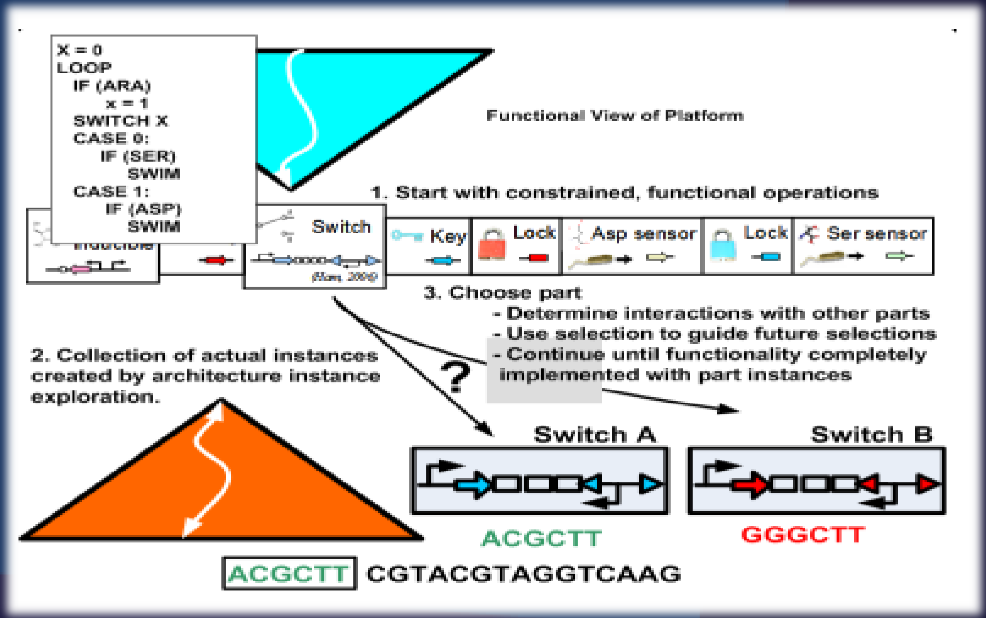




- Clotho is a design environment for the creation of biological systems from standardized biological parts.
- Composed of “views”, “connectors”, “interfaces” and “tools”
- iGEM 2008, 2009, 2011 Winner “Best Software Tool” and Gold Medal 2008,2009,2011, 2012.
- Versions available at *http://cidarlab.org/software-overview/.*



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Putting it all together

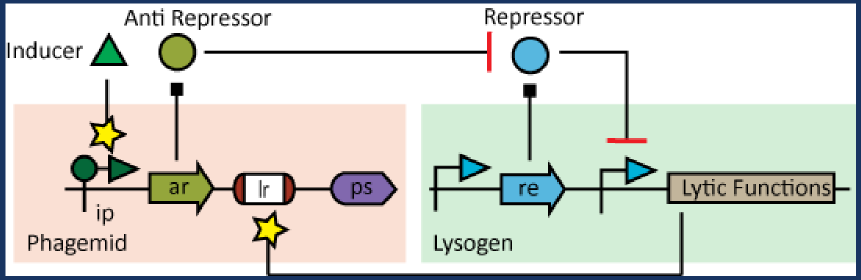
(Doug Densmore, Boston University)

1. Decide on the general functionality desired.

2. Specify the composition of the devices and the constraints on the system.

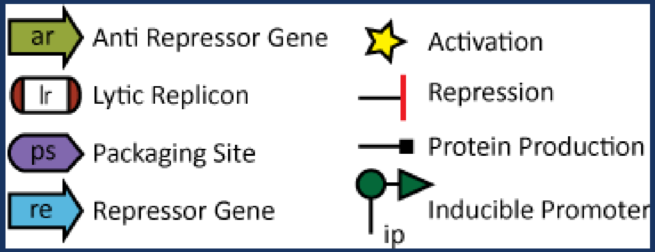
3. Design variations of the design, assign theoretical parts to physical samples, modify sequence, etc.

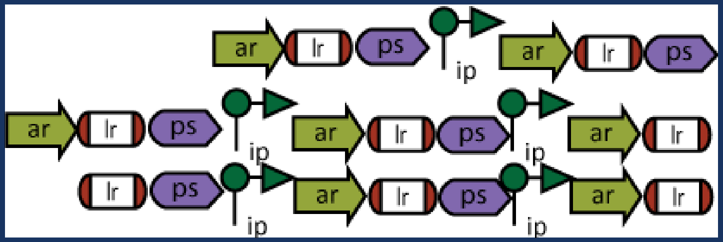
4. Send design to liquid handling robot assembly workflows, capture successes and failures as constraints for future designs, and save created devices.

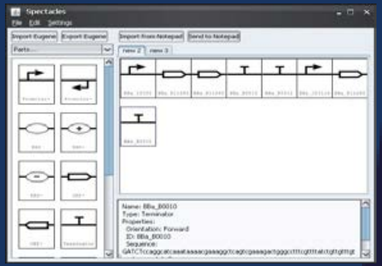


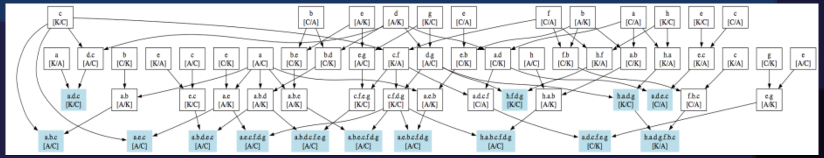

```
InduciblePromoter ip("ACTGGT…");
AntiRepressor ar("CATGGT…", "high");
Terminator t("GGTAAC…", 99);
LyticReplicon lr("CTTACC…", 110);
```

```
Rule r4a(rp1 NOTWITH lr);
Note(r4a);
```









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Industry Landscape

	Drug Discovery					Drug Development			
Leading Players	Schrödinger, Chemical Computing Group, Dassault Systèmes, OpenEye					Certara, SimulationsPlus, Dassault Systèmes			
Phase	Target Identification & Validation	Hit Discovery	Hit to Lead	Lead Optimization	Clinical Candidate	Preclinical discovery	Investigational New Drug (IND)	Clinical Trials	New Drug Application (NDA)
Duration	2-3 years	0.5-1 year	1-2 years	1-2 years		1-2 years		4-8 years	
R&D Cost (one drug)	$100M	$94M	$166M	$414M		$150M		$906M	
Modeling & Simulations use model	• Understand Protein function and dynamics	• Targeted search • Library screening	• Refine search • Property prediction	• Improve properties • Crystal structure prediction		• Drug solubility • Physiological response prediction		• Trial design and planning • Virtual Clinical Trials	

Improvements in speed, accuracy and usability of simulations will drive broader adoption and help Pharma to move to a more robust methodology and to a "fail fast, fail cheap" model

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Final Words of Wisdom

Giuseppe Arcimboldo, The Librarian, 1566
Skokloster Castle, Sweden

Giorgio De Chirico, Le Muse Inquietanti, 1917-18
Collezione Mattioli, Milano, Italy

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Concluding Remarks

- It has been a long and wonderful journey … more than 45 years!
- But it is not over … yet! Much needs to be done…
- PRINCIPLES MUST guide research, NOT techniques
- We need new paradigms to go beyond what we know:
  - Cyber-physical systems, Systems of systems…, Swarm systems
  - Biological Systems
- Education!

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By Popular request (Ant):

IS ARTIFICIAL INTELLIGENCE A PANACEA?

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Big Data + Processing Power =

New Age for Artificial Intelligence

[Source: www.cbinsights.com](http://www.cbinsights.com)

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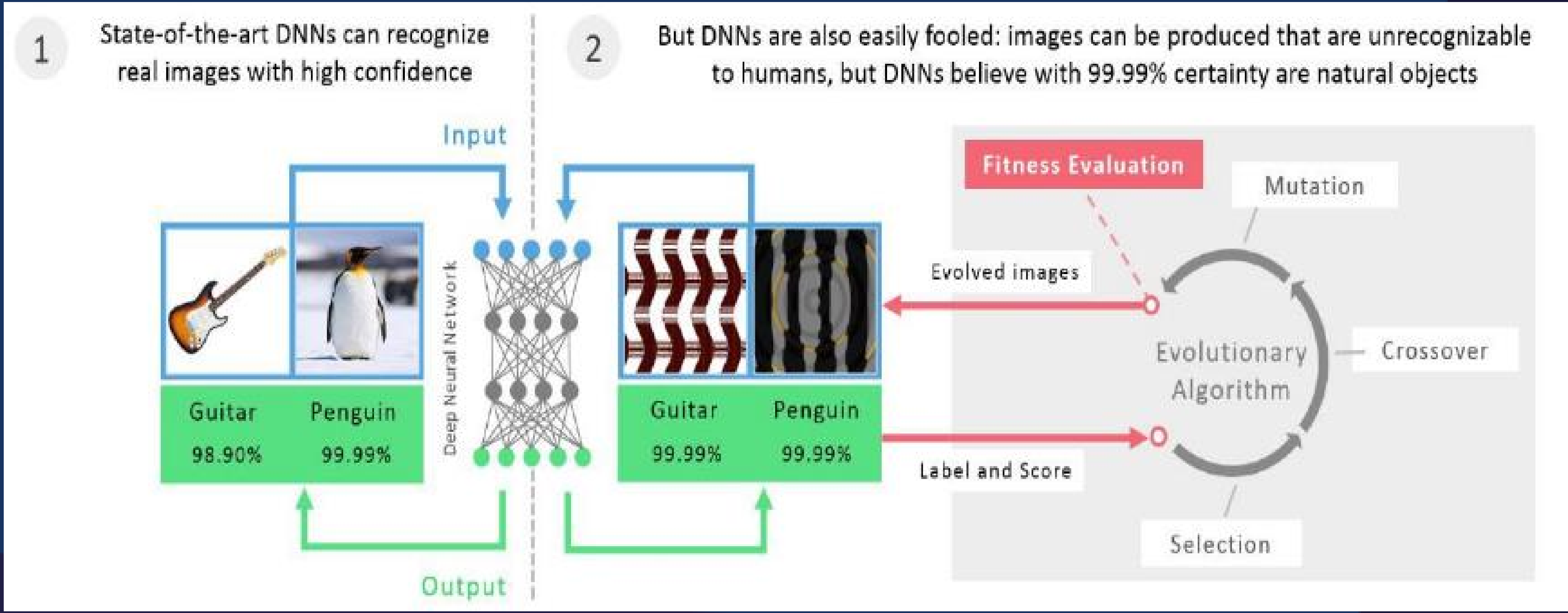
A Convolutional Neural Network can be fooled…



[images from https://arxiv.org/pdf/1412.1897v4.pdf]

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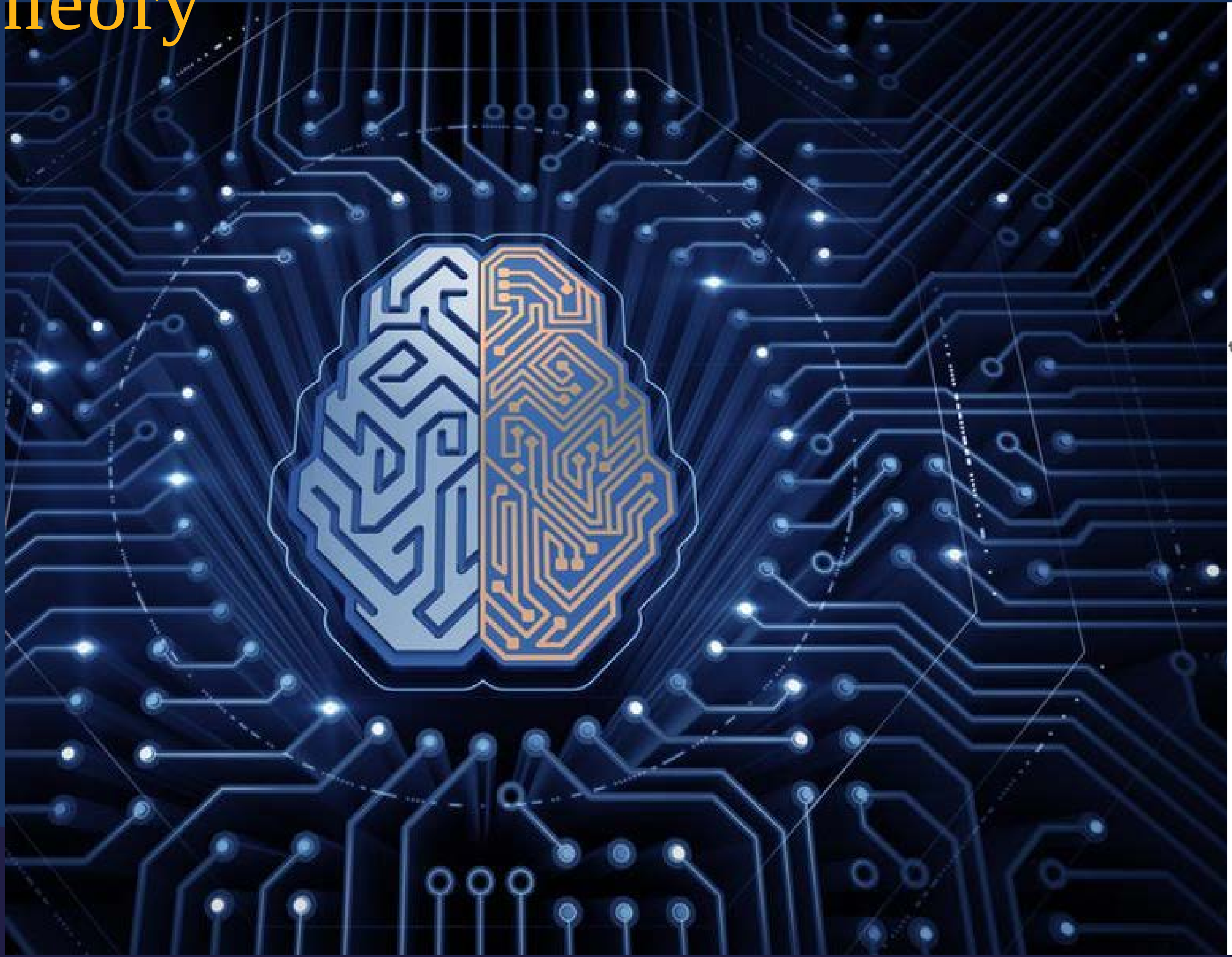
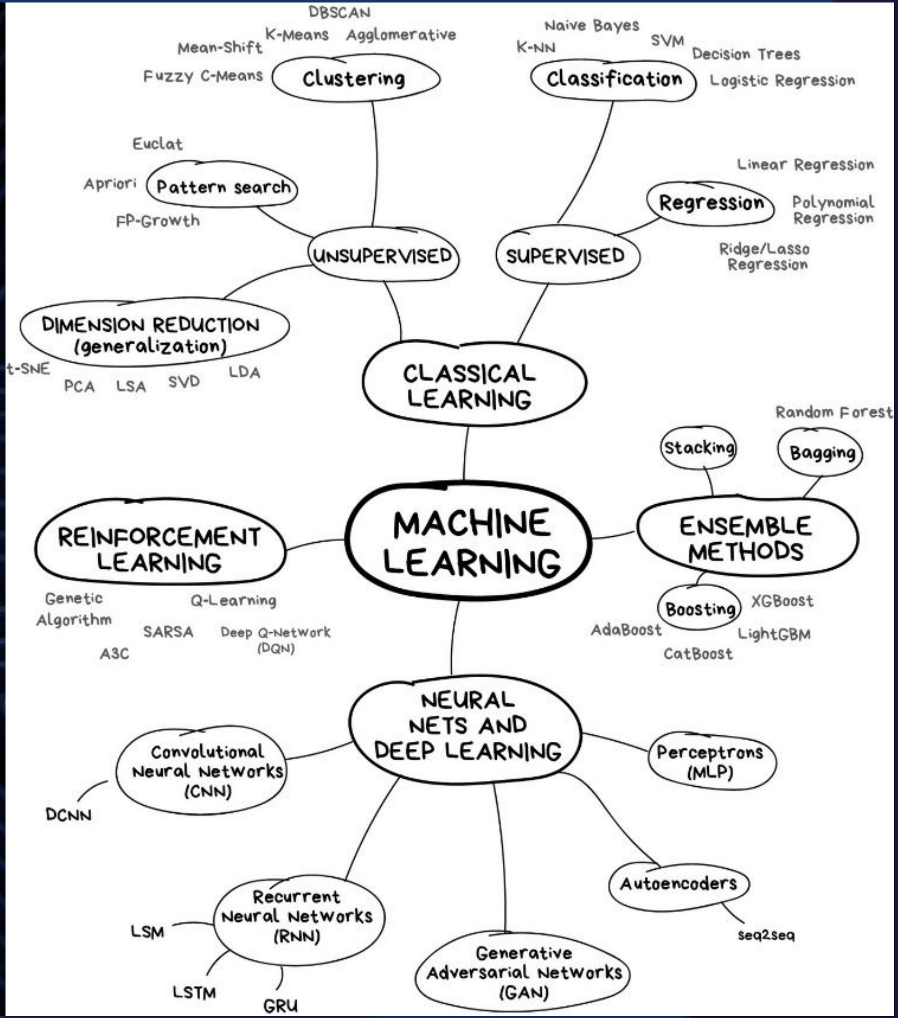
Bottom line: AI/ML is Glorified Statistics/Approximation Theory





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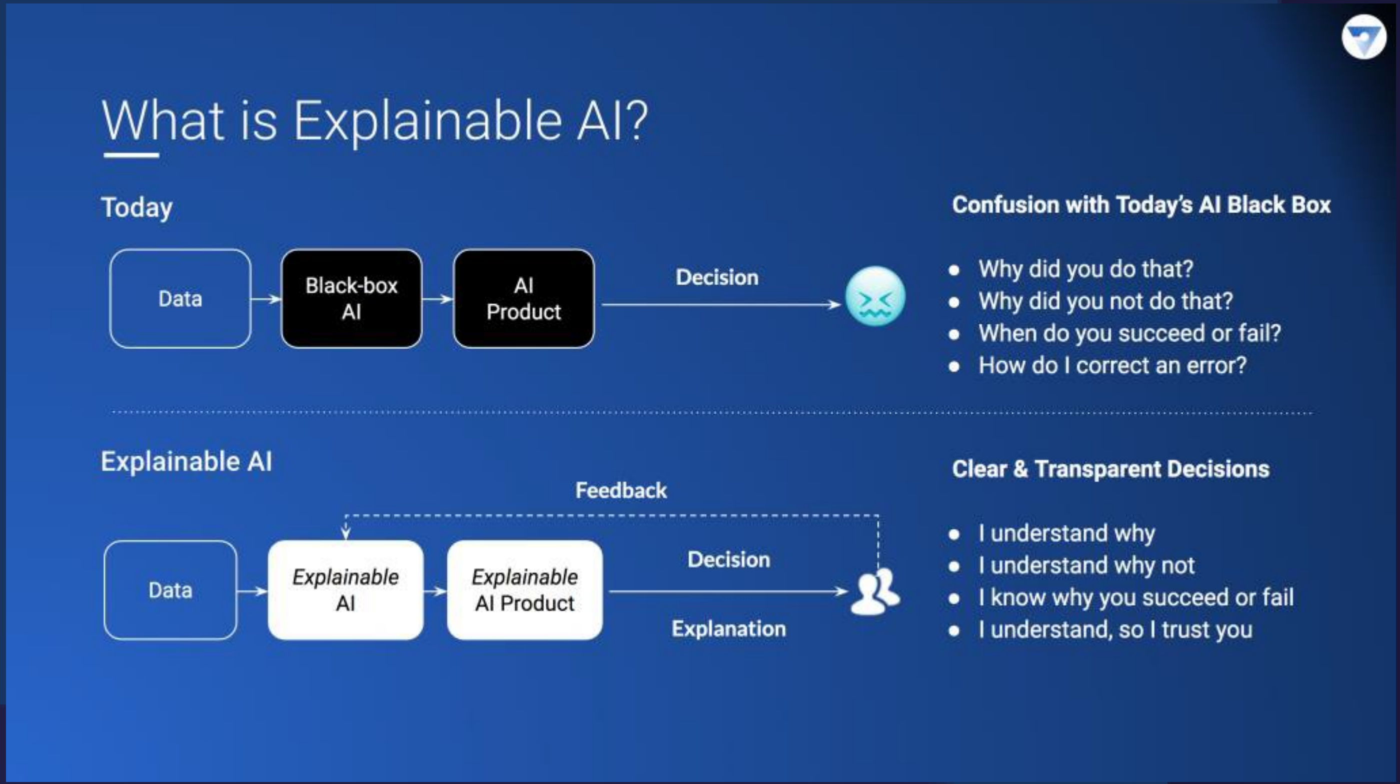
Concerns around AI biases are mounting

AI transparency tech, also known as explainable AI, traces back outputs from AI algorithms to provide a way to understand what's happening in "human terms."

As AI is increasingly used for decision-making across industries, **understanding how and why** an algorithm makes its decisions can **help mitigate inherent biases** associated with most AI systems in existence today.



Source: Fiddler Labs

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