NVIDIA

AI REVOLUTION BEGINS

Ryan Shen | Solution Architect | AI For Industry

Aug, 2018

Key components

AI Revolution begins

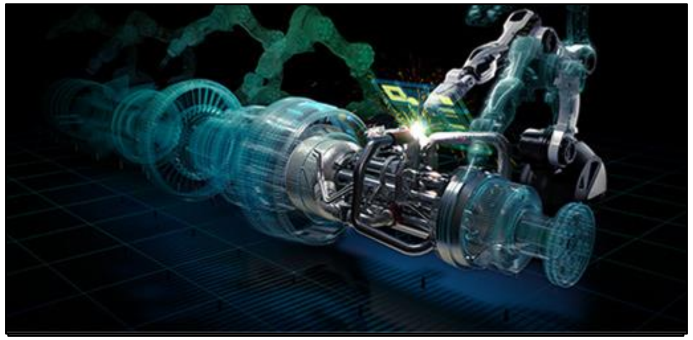
Why NVIDIA

Artificial Intelligence

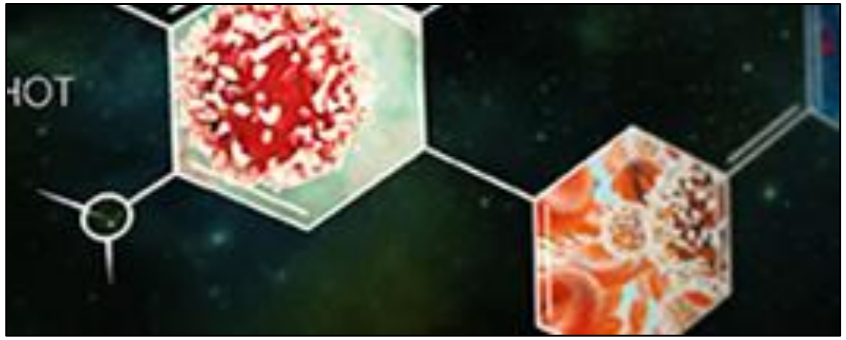
AI Transportation

Taiwan ecosystem opportunity

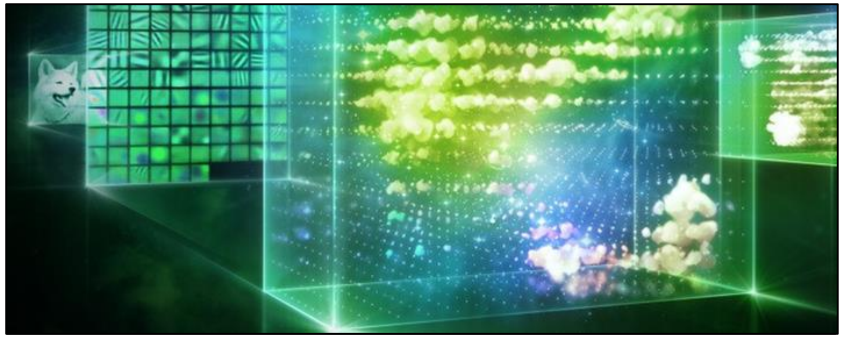
DEEP LEARNING IS SWEEPING ACROSS INDUSTRIES



Robotics
Manufacturing, construction, navigation

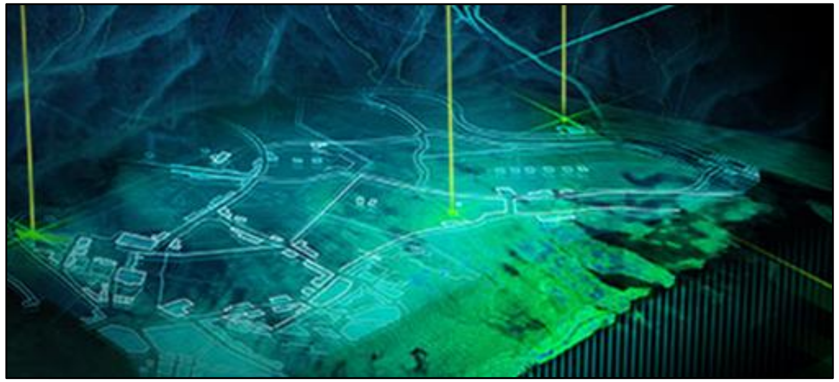


Healthcare
Cancer detection, drug discovery, genomics

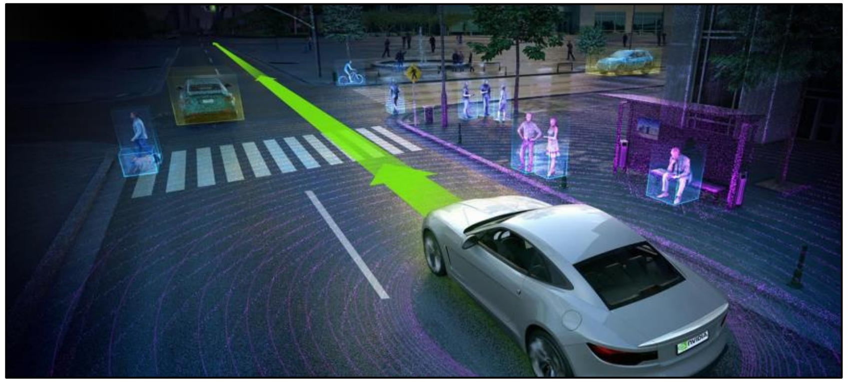


Internet services
Image classification, speech recognition, NLP

Finance
Trading strategy, fraud detection



Security & Defense
Face recognition, video surveillance, cybersecurity

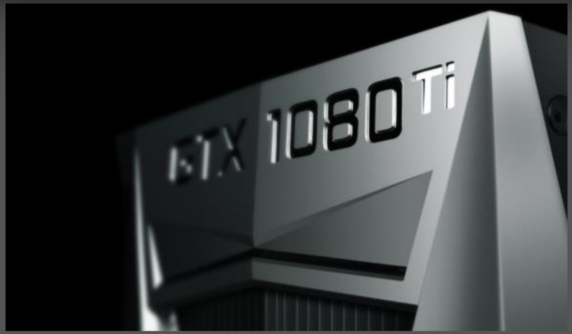


Autonomous Vehicles
Pedestrian & traffic sign detection, lane tracking

Key components

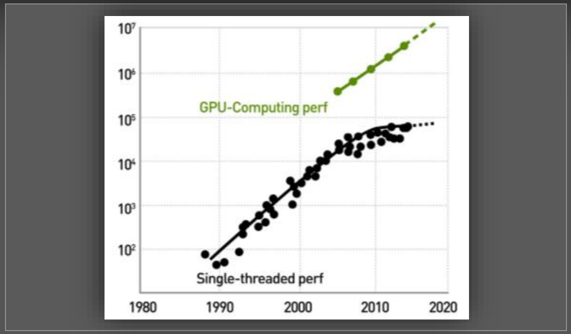
- AI Revolution begins
- Why NVIDIA
- Artificial Intelligence
- AI Transportation
- Taiwan ecosystem opportunity

NVIDIA — "THE AI COMPUTING COMPANY"



#1 PC Gaming

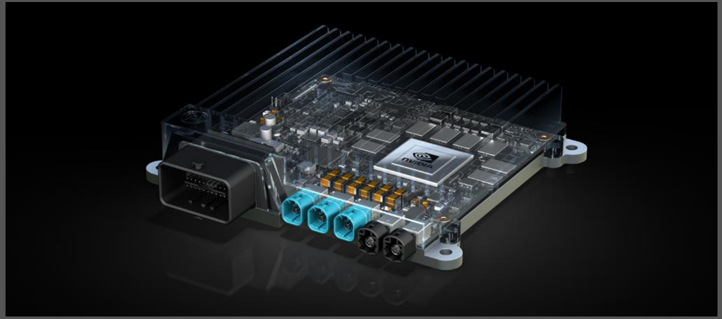
#1 Pro Graphics



#1 Accelerated Computing

#1 AI Computing

Fastest Supercomputers in Japan, U.S., Europe



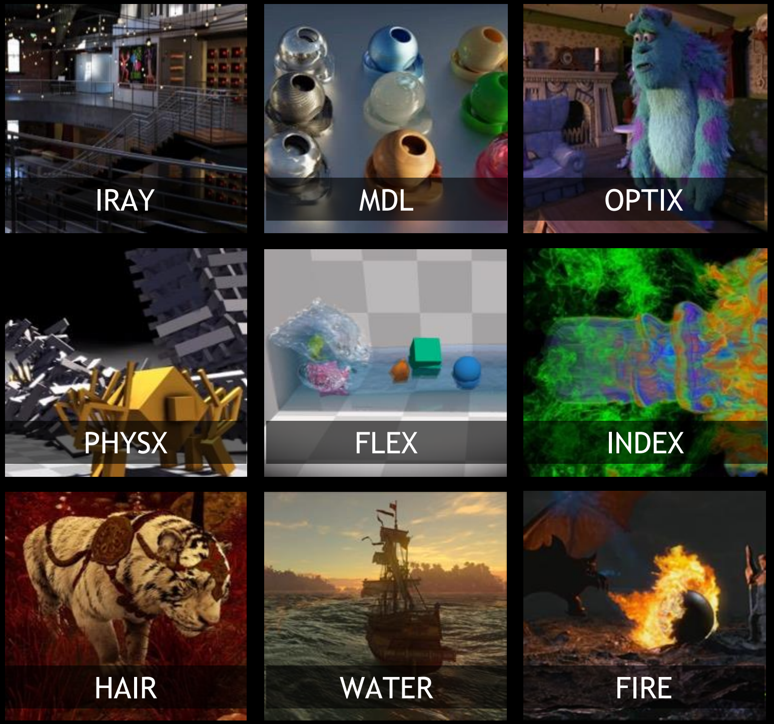
Pioneering AI Car Computer

Nintendo Switch

Founded in 1993 — 11,500 employees | Invented the GPU | Invented GPU-accelerated computing

NVIDIA PLATFORM SOFTWARE

GRAPHICS



HPC

Applications

- **NekCEM** Computational Electromagnetics
- **COSMO** Climate Weather
- **CloverLeaf** CFD
- **MAESTRO CASTRO** Astrophysics
- **LSDalton** Quantum Chemistry
- **Numeca** CFD
- **PowerGrid** Medical Imagi
- **INCOMP3D** CFD

AI

Deep Learning Frameworks

Caffe
Microsoft CNTK
mxnet
TensorFlow
theano
torch

NVIDIA GPU-computing SDK

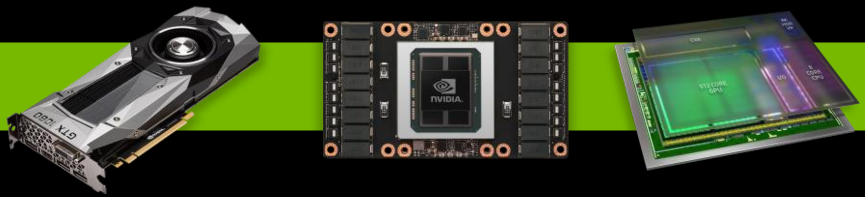
cuDNN
TensorRT
DeepStream SDK
cuBLAS
cuSPARSE
NCCL

GPU0 GPU1 GPU3 GPU2

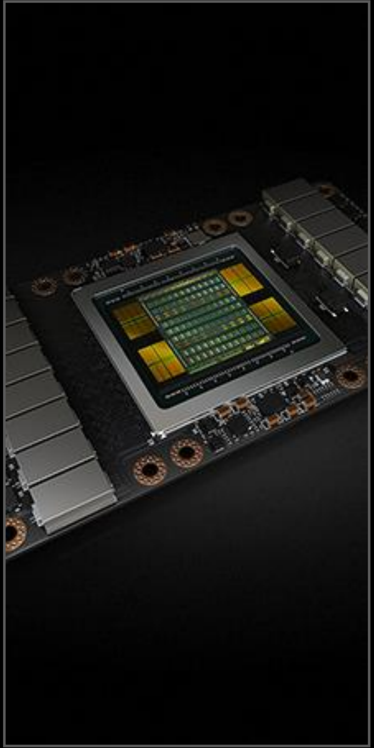
NVDEC Inference NVENC

amazon web services
Google Cloud Platform
Microsoft Azure
DELL
Hewlett Packard Enterprise
IBM

OpenGL, DirectX, CUDA



NVIDIA AI PLATFORM



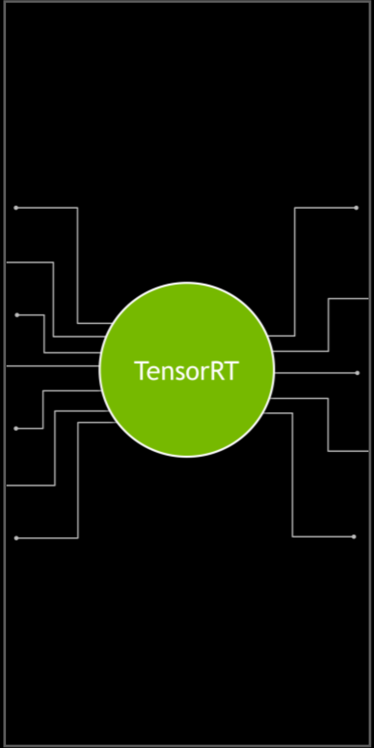
Tesla V100
NEW 32GB

DGX Systems
NEW with V100 32GB
NEW DGX-2

Alibaba Cloud
aws
Baidu Cloud
Google Cloud
Microsoft Azure
ORACLE
Tencent Cloud
CISCO
CRAY
DELL EMC
Hewlett Packard Enterprise
IBM
Lenovo

Every Cloud
NGC Now on AWS, GCP, AliCloud, Oracle

NVIDIA GPU Cloud
30 GPU-Optimized Containers

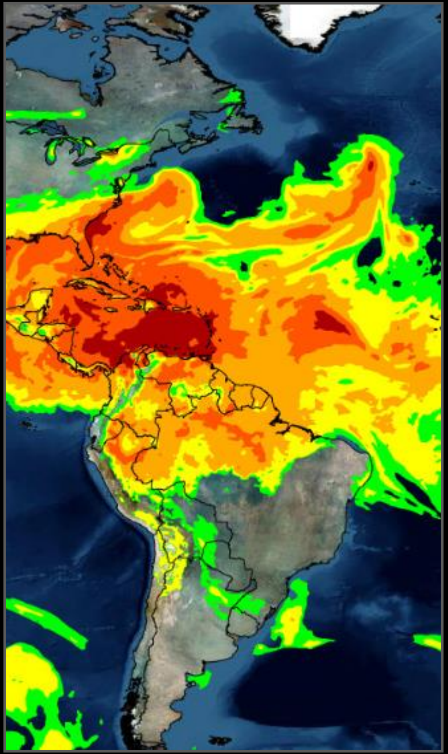


NVIDIA AI Inference
NEW TensorRT 4, TensorFlow Kaldi, ONNX, WinML

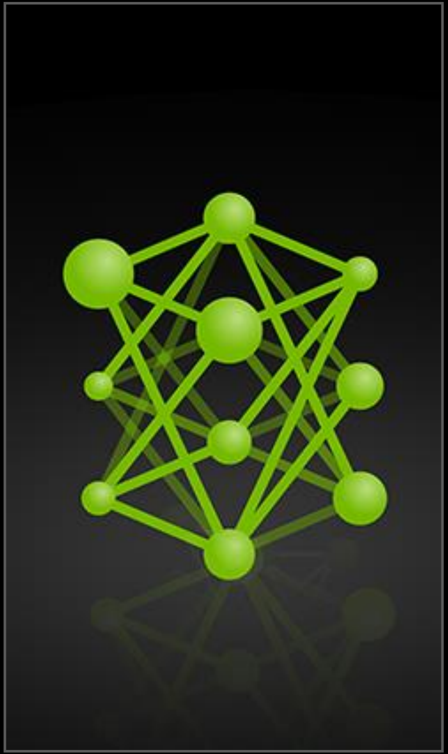
TITAN V
Supercomputer for Developers

"NVIDIA's AI Prowess Could Lead to an Outsized Share in the Growing Data Center and AI Markets"

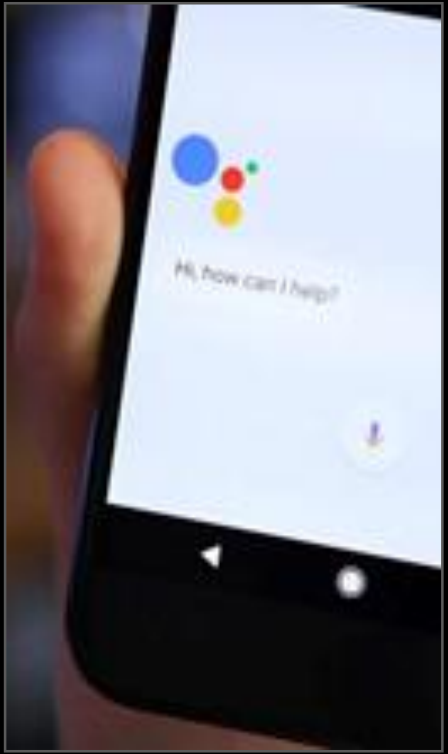
— Business Insider



High Performance Computing

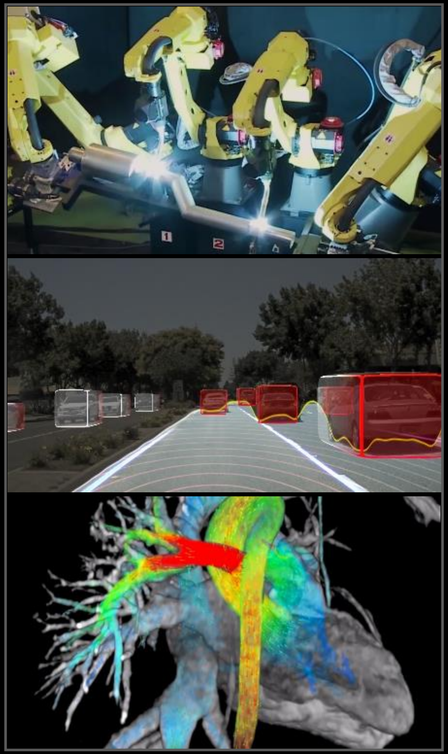


Hyperscale Training



Hyperscale Inference

Cloud Computing



Vertical Industries

Key components

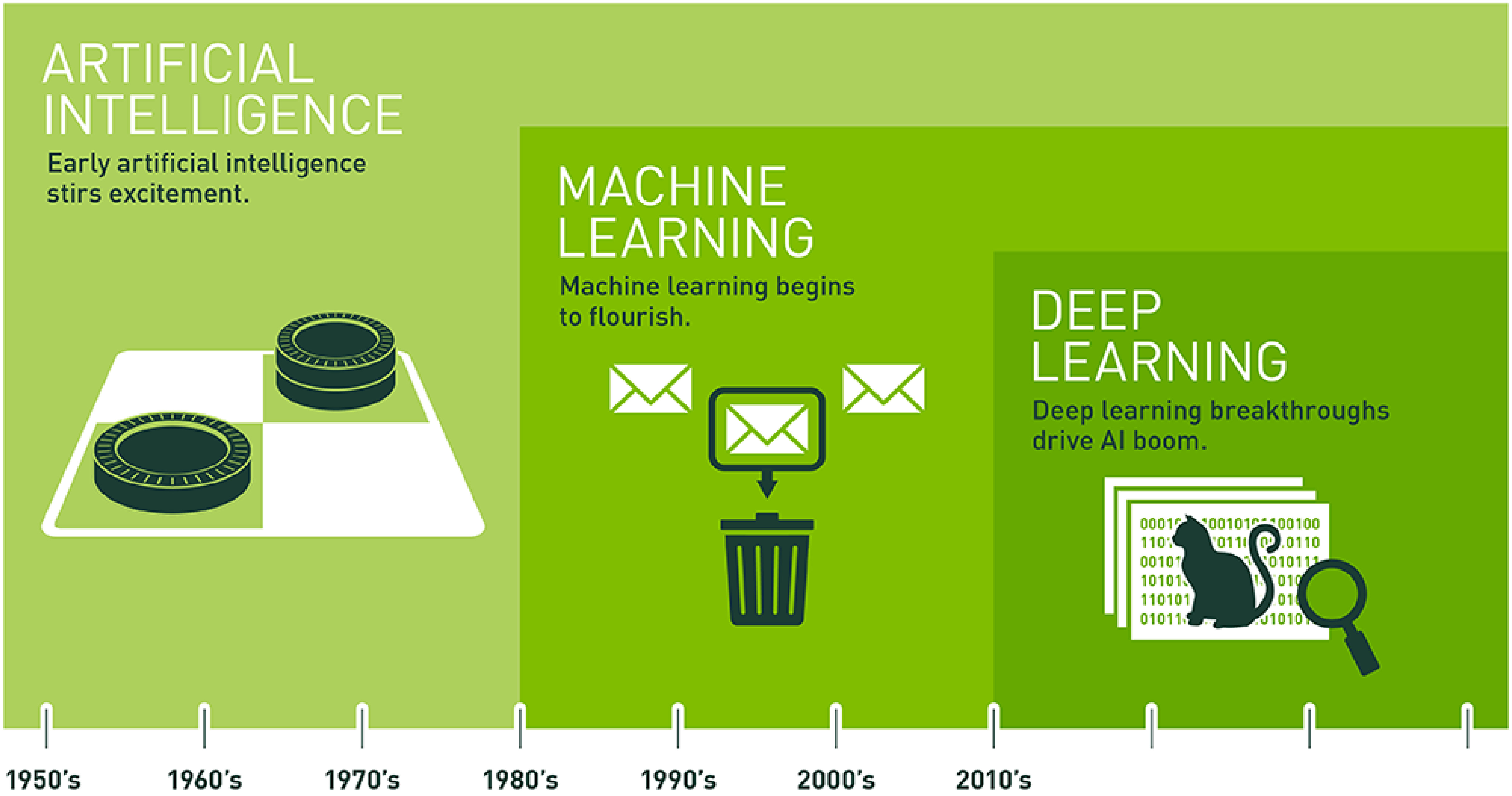
AI Revolution begins

Why NVIDIA

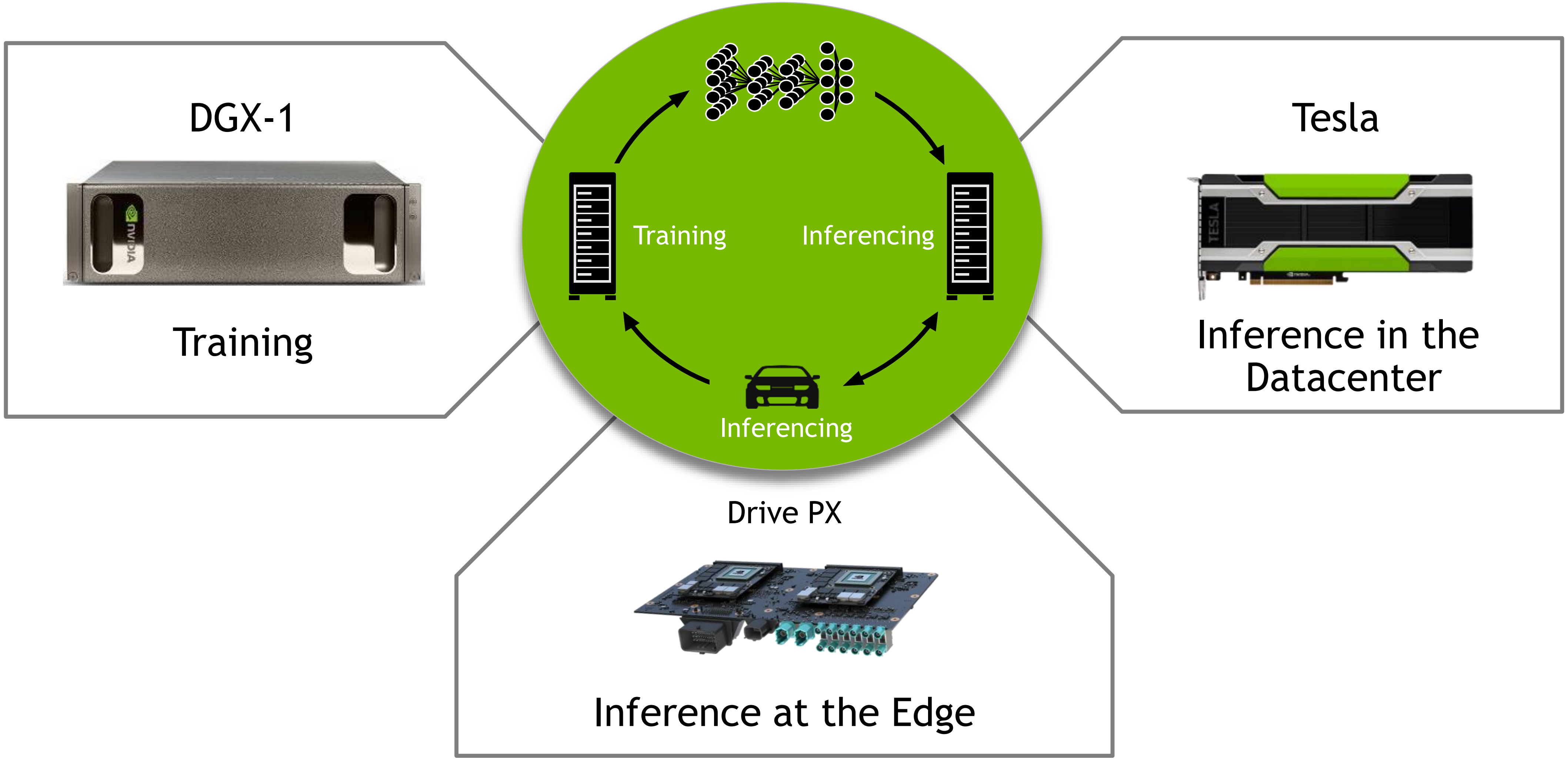
Artificial Intelligence

AI Transportation

Taiwan ecosystem opportunity


ARTIFICIAL INTELLIGENCE
Early artificial intelligence stirs excitement.
MACHINE LEARNING
Machine learning begins to flourish.
DEEP LEARNING
Deep learning breakthroughs drive AI boom.
1950's
1960's
1970's
1980's
1990's
2000's
2010's

GPU DEEP LEARNING IS A NEW COMPUTING MODEL



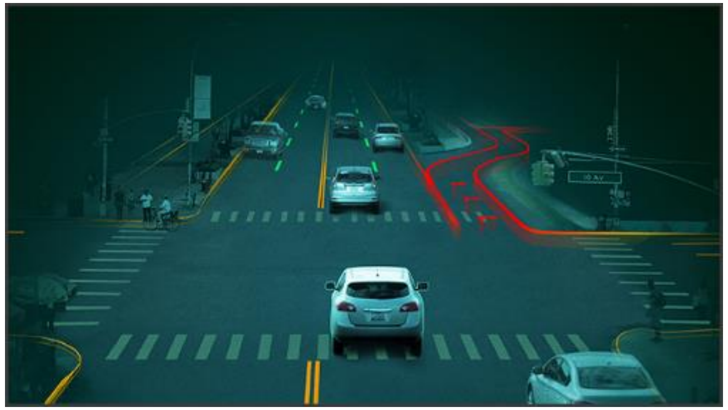
AI IS THE SOLUTION TO SELF-DRIVING

Perception

Reasoning

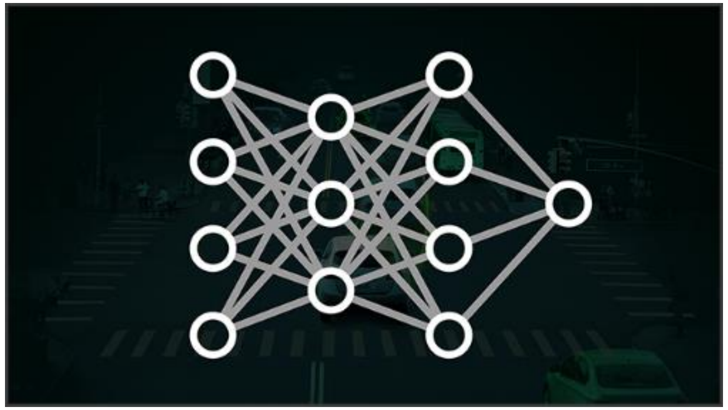
Prediction

Localization & Planning



HD Map Creation

AI Computing



Key components

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EVERYTHING THAT MOVES WILL BE AUTONOMOUS

Cars

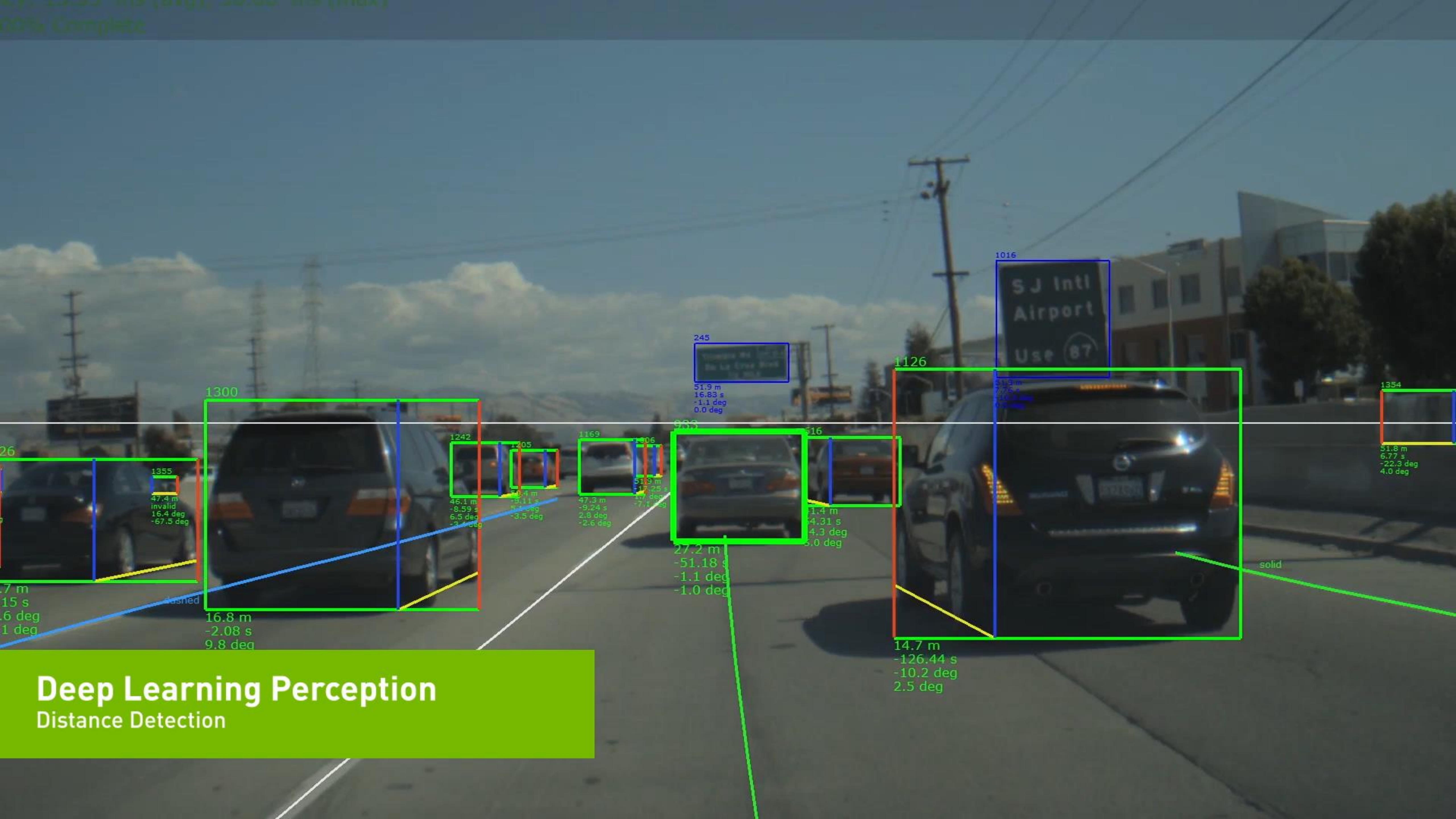
Robotaxis

Trucks

Delivery Vans

Buses

Tractors


Deep Learning Perception
Distance Detection
SJ Intl
Airport
Use 87
1300
16.8 m
-2.08 s
9.8 deg
1126
14.7 m
-126.44 s
-10.2 deg
2.5 deg
27.2 m
-51.18 s
-1.1 deg
-1.0 deg
solid
dashed

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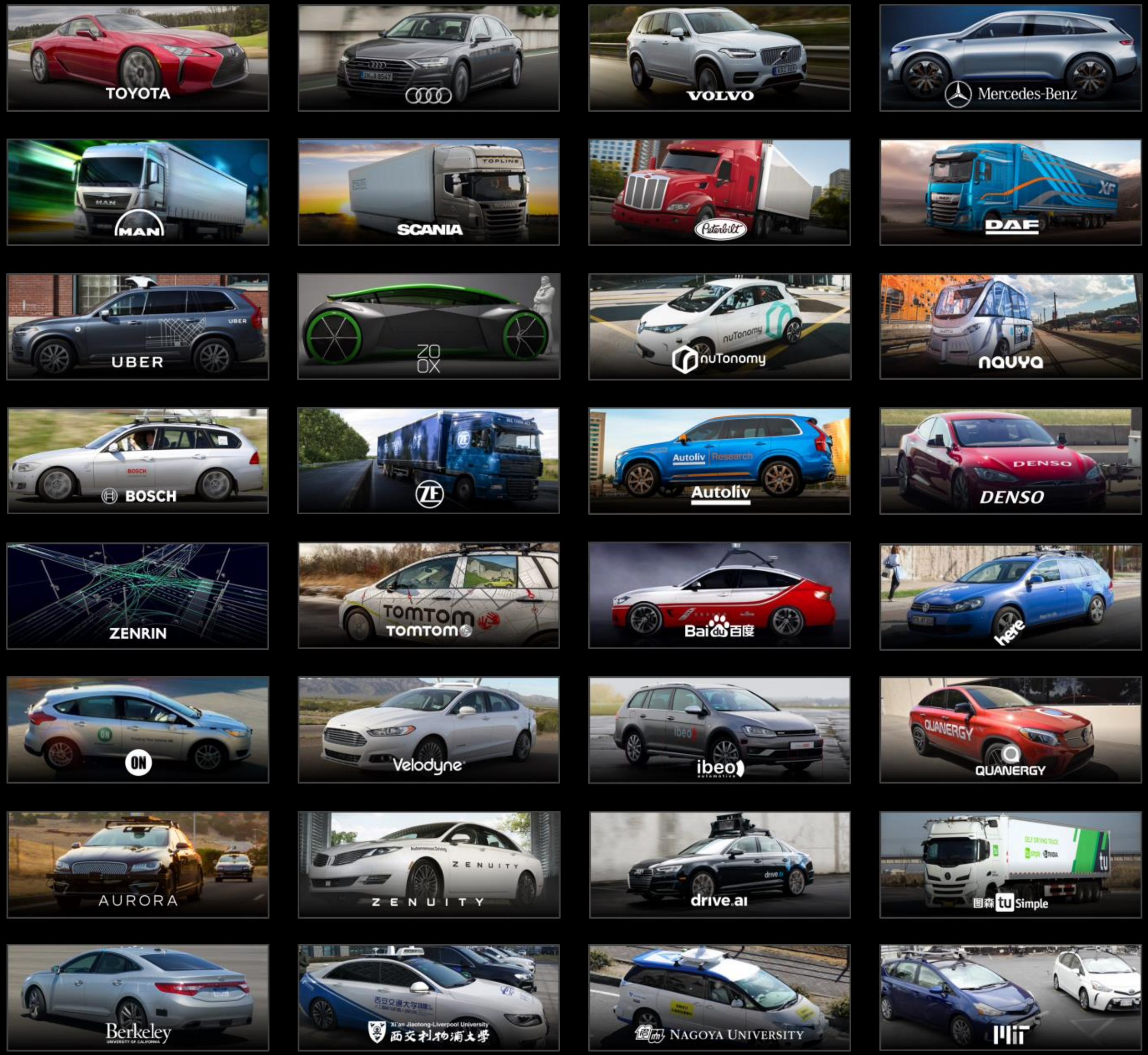
TAIWAN ECOSYSTEM

THE POWER OF AN OPEN PLATFORM

370+ PARTNERS DEVELOPING ON NVIDIA DRIVE



CARS

TRUCKS

MOBILITY SERVICES

SUPPLIERS

MAPPING

SENSORS

STARTUPS

RESEARCH

INVENTING THE FUTURE


XAVIER IS HERE

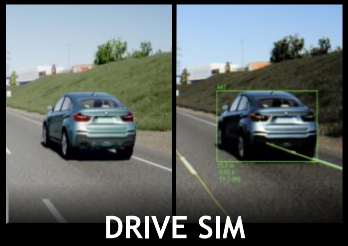

DRIVE PEGASUS

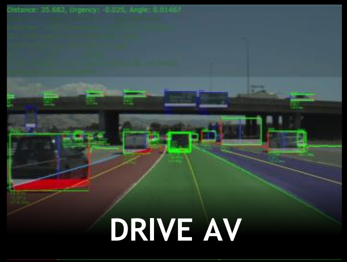

VW AI


BAIDU APOLLO


AUDI DEPLOYS ZFAS

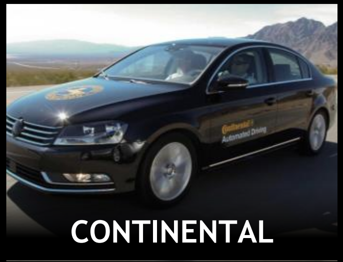

MERCEDES-BENZ AI


DRIVE SIM


DRIVE AV

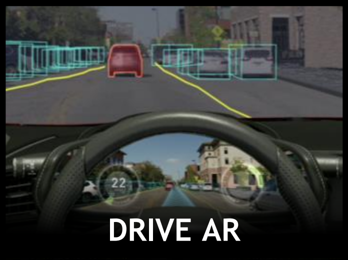

VOLVO / AUTOLIV


AURORA


CONTINENTAL


DEUTSCHE POST DHL


DRIVE IX


DRIVE AR


ZF / CHERY


UBER


TUSIMPLE


PACCAR

PRODUCTS

PARTNERS

NVIDIA®

NVIDIA DEEP LEARNING INSTITUTE

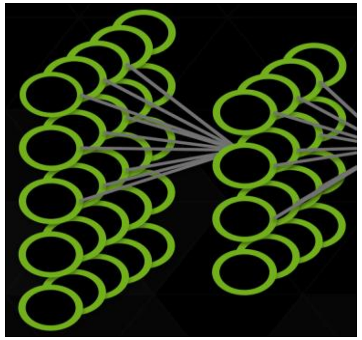
Hands-on self-paced and instructor-led training in deep learning and accelerated computing for developers

Request onsite instructor-led workshops at your organization: **www.nvidia.com/requestdli**

Take self-paced labs online: **www.nvidia.com/dlilabs**

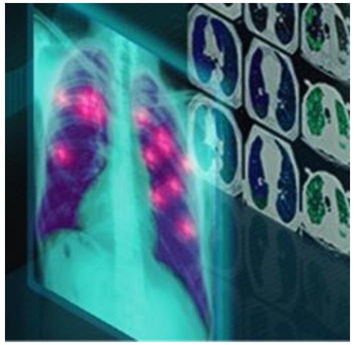
Download the course catalog, view upcoming workshops, and learn about the University Ambassador Program: **www.nvidia.com/dli**

Caffe2 · Microsoft Cognitive Toolkit · mxnet · TensorFlow · PYTORCH

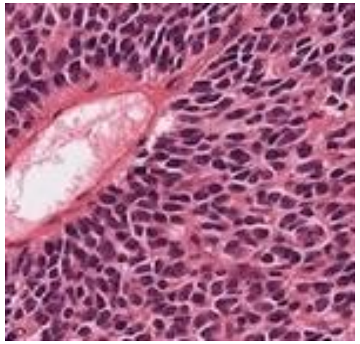


Deep Learning Fundamentals

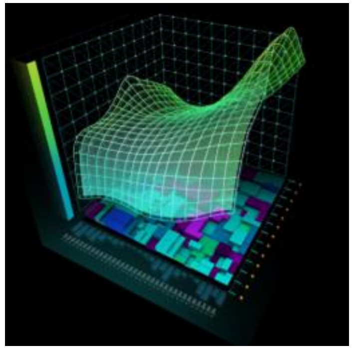
Autonomous Vehicles



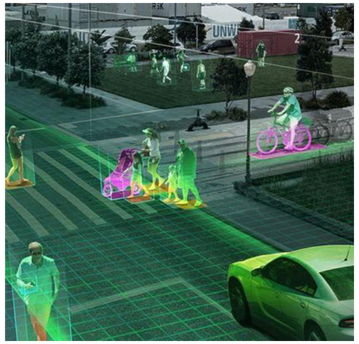
Medical Image Analysis



Genomics

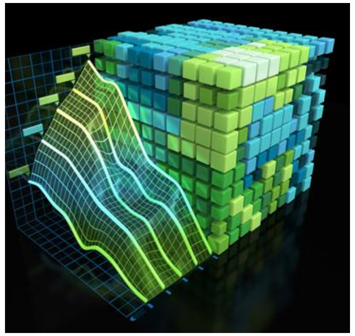


Finance



Intelligent Video Analytics

Game Development & Digital Content



Accelerated Computing Fundamentals

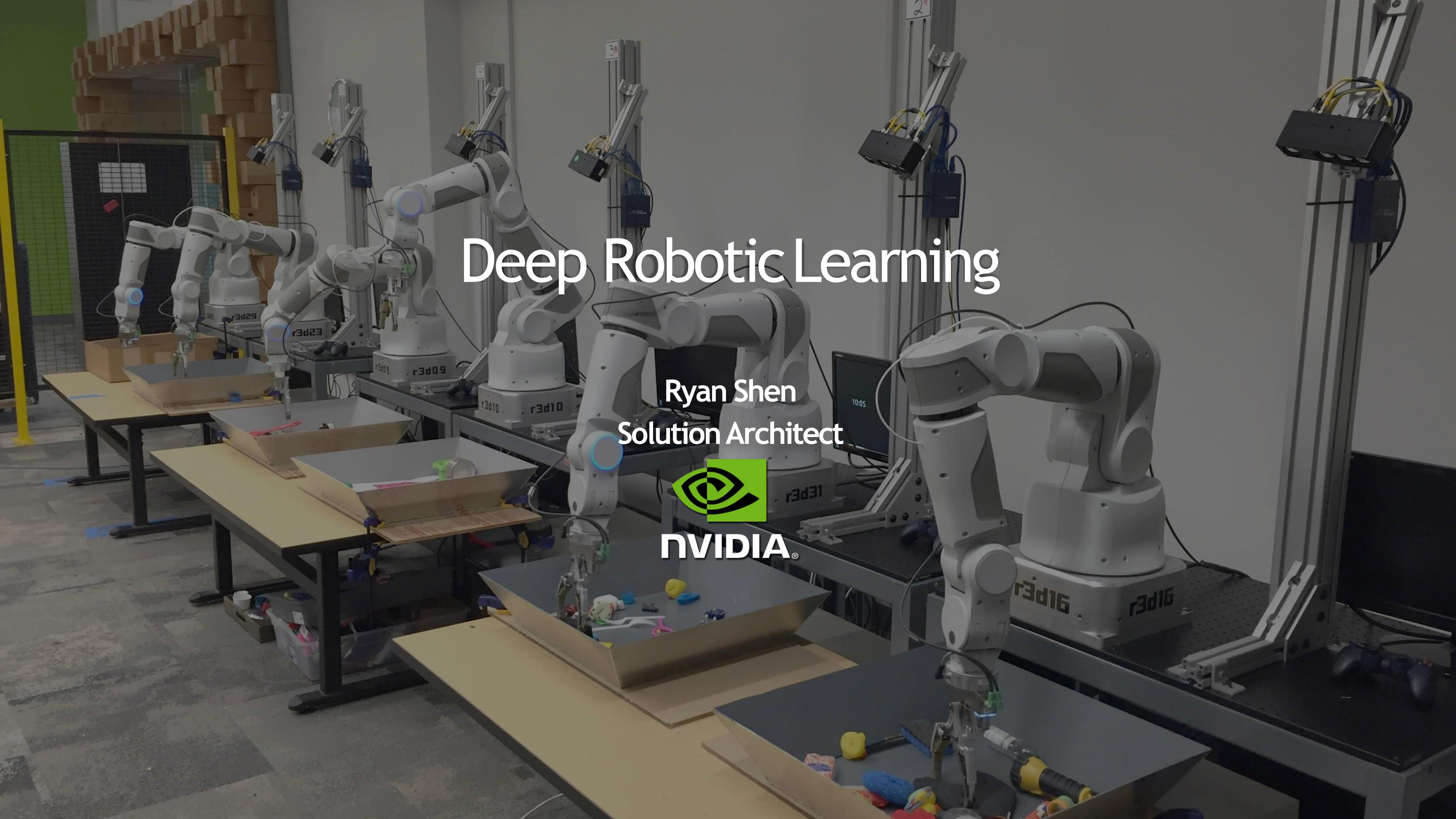
More industry-specific training coming soon…

NVIDIA DEEP LEARNING INSTITUTE

Deep Robotic Learning

Ryan Shen
Solution Architect

NVIDIA

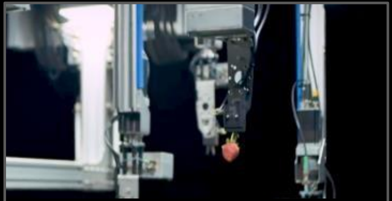


FEW YEARS AGO...

BILLIONS OF INTELLIGENT MACHINES

DELIVERY

INDUSTRIAL DRONES



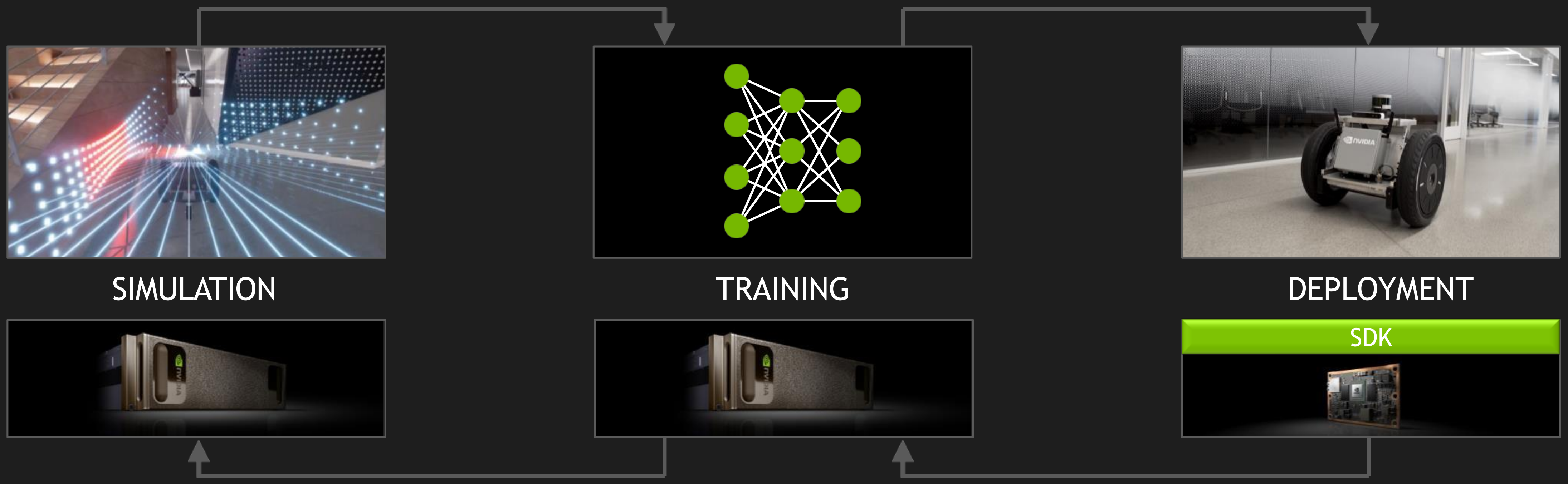
AGRICULTURE

PICK-AND-PLACE

LOGISTICS

MANUFACTURING

NVIDIA ISAAC ROBOTICS PLATFORM



ANNOUNCING: JETSON XAVIER

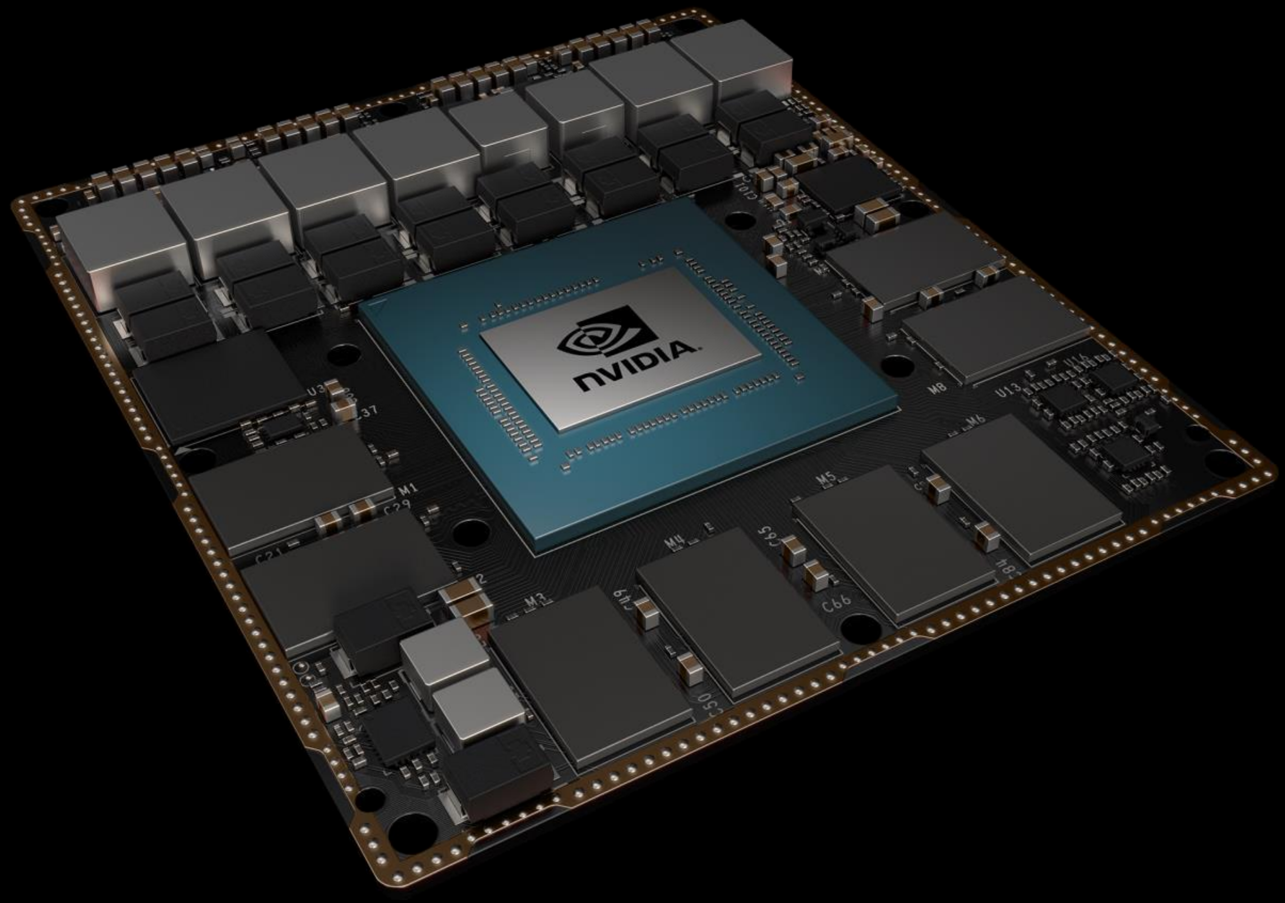
Computer for Autonomous Machines

AI Server Performance in 30W • 15W • 10W

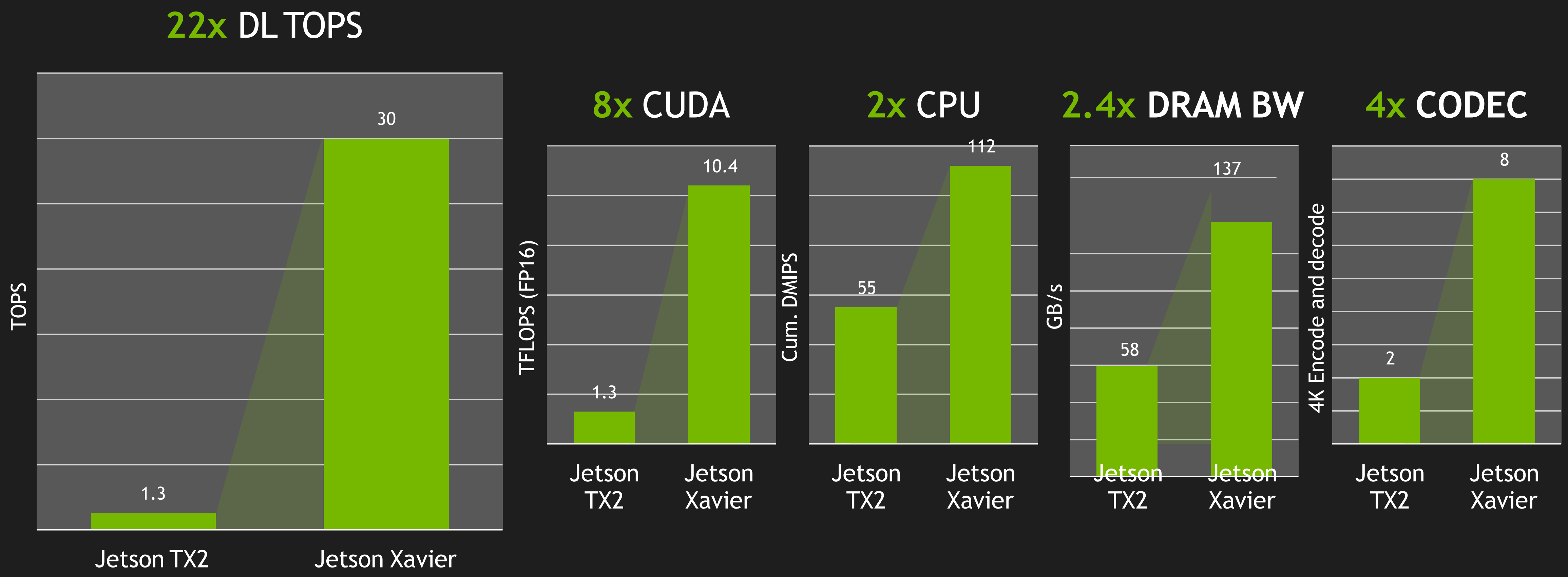
512 Volta CUDA Cores • 2x NVDLA

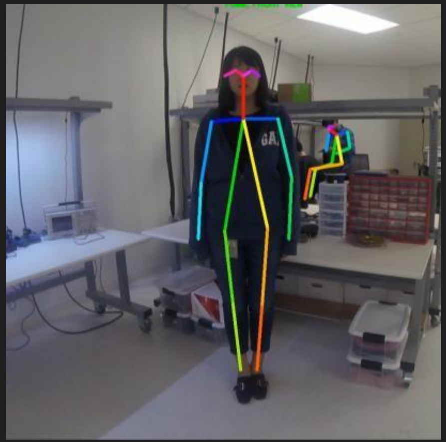
8 core CPU

30 DL TOPS

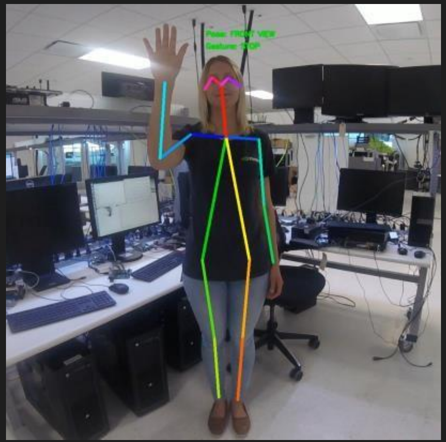


JETSON XAVIER
20X PERFORMANCE IN 2 YEARS

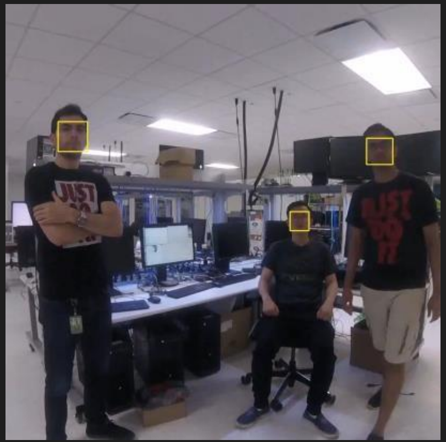




POSE



GESTURE

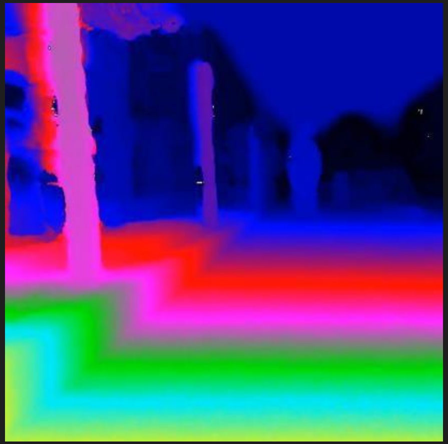


FACE REC & TRACKING

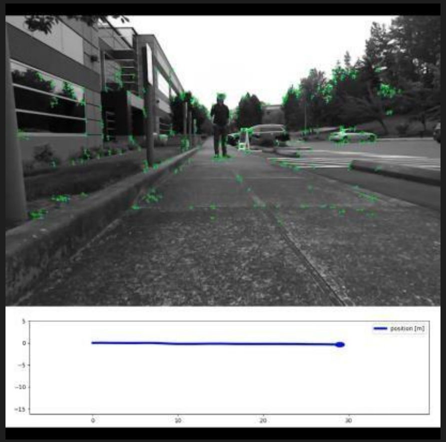
SPEECH

EYE TRACKING

HAND POSE



DEPTH



VISUAL ODOMETRY

ISAAC IMX (Intelligent Machine Acceleration Applications)

JETSON XAVIER DEVELOPER KIT

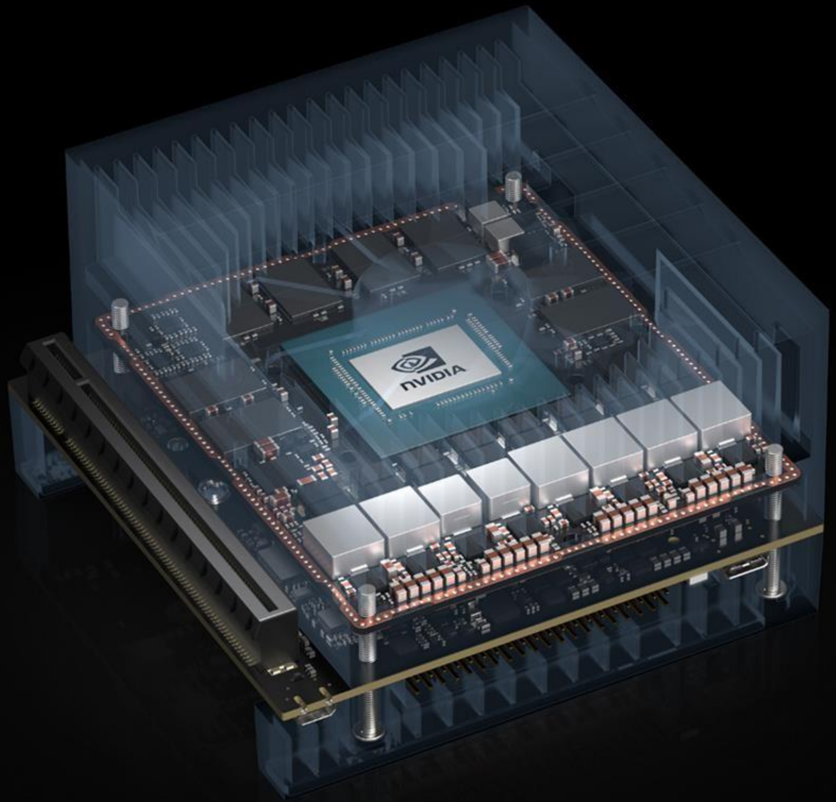
Available from distributors WW

Early access August 2018

JETSON XAVIER DEVELOPER KIT

Available from distributors WW

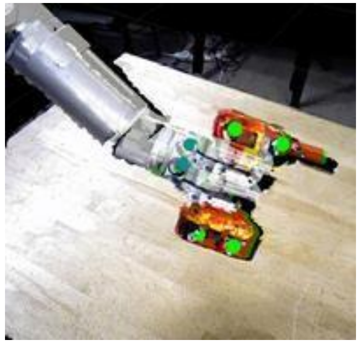
Early access August 2018

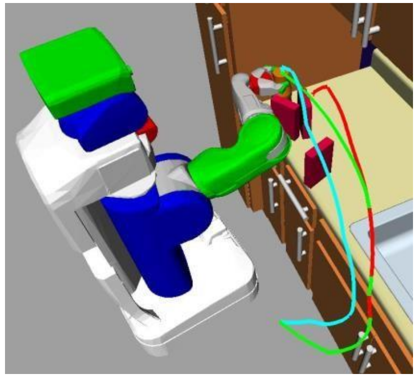


INTELLIGENT MACHINES

"Billions of intelligent devices will take advantage of DNNs to provide personalization and localization as GPUs become faster and faster over the next several years."

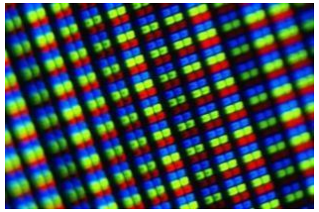
— Tractica

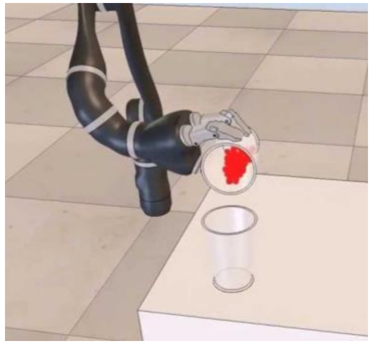


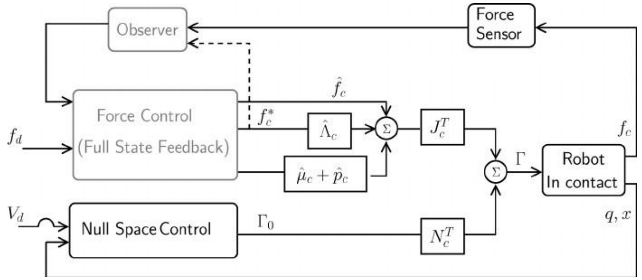


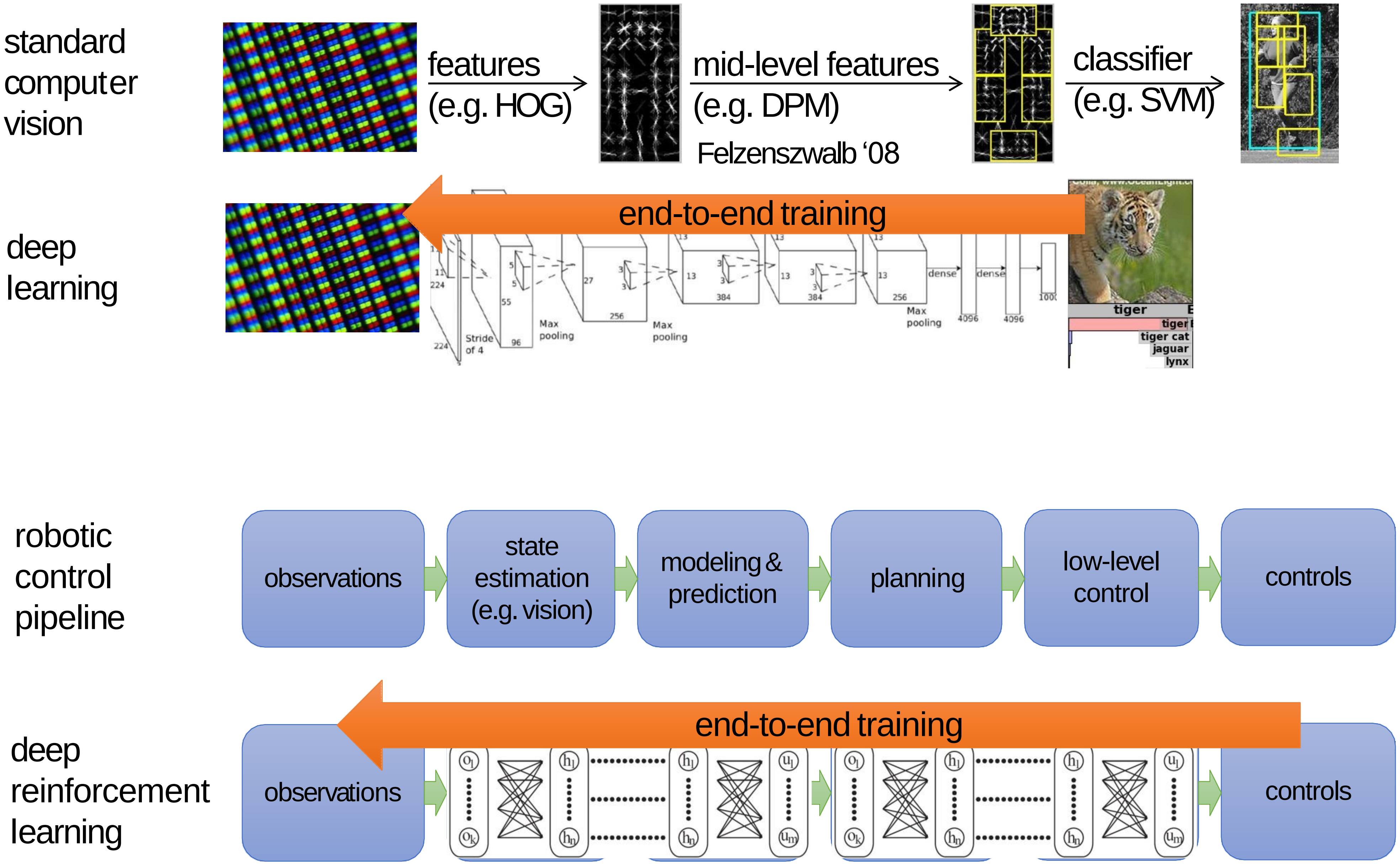
robotic
control
pipeline

observations → state estimation (e.g. vision) → modeling & prediction → planning → low-level control → controls



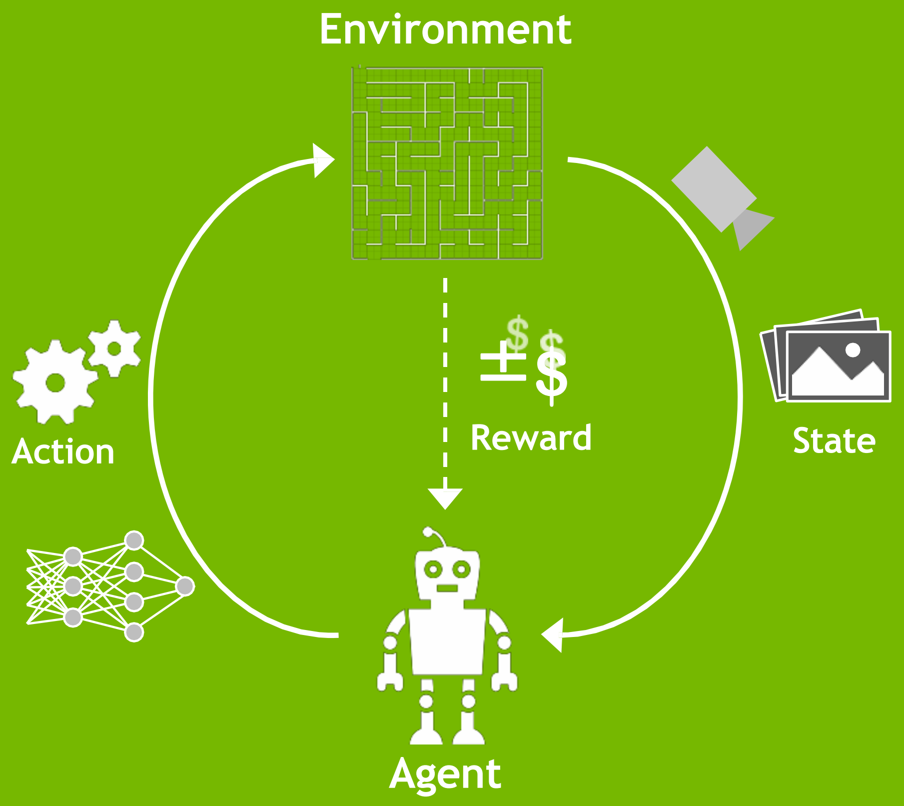




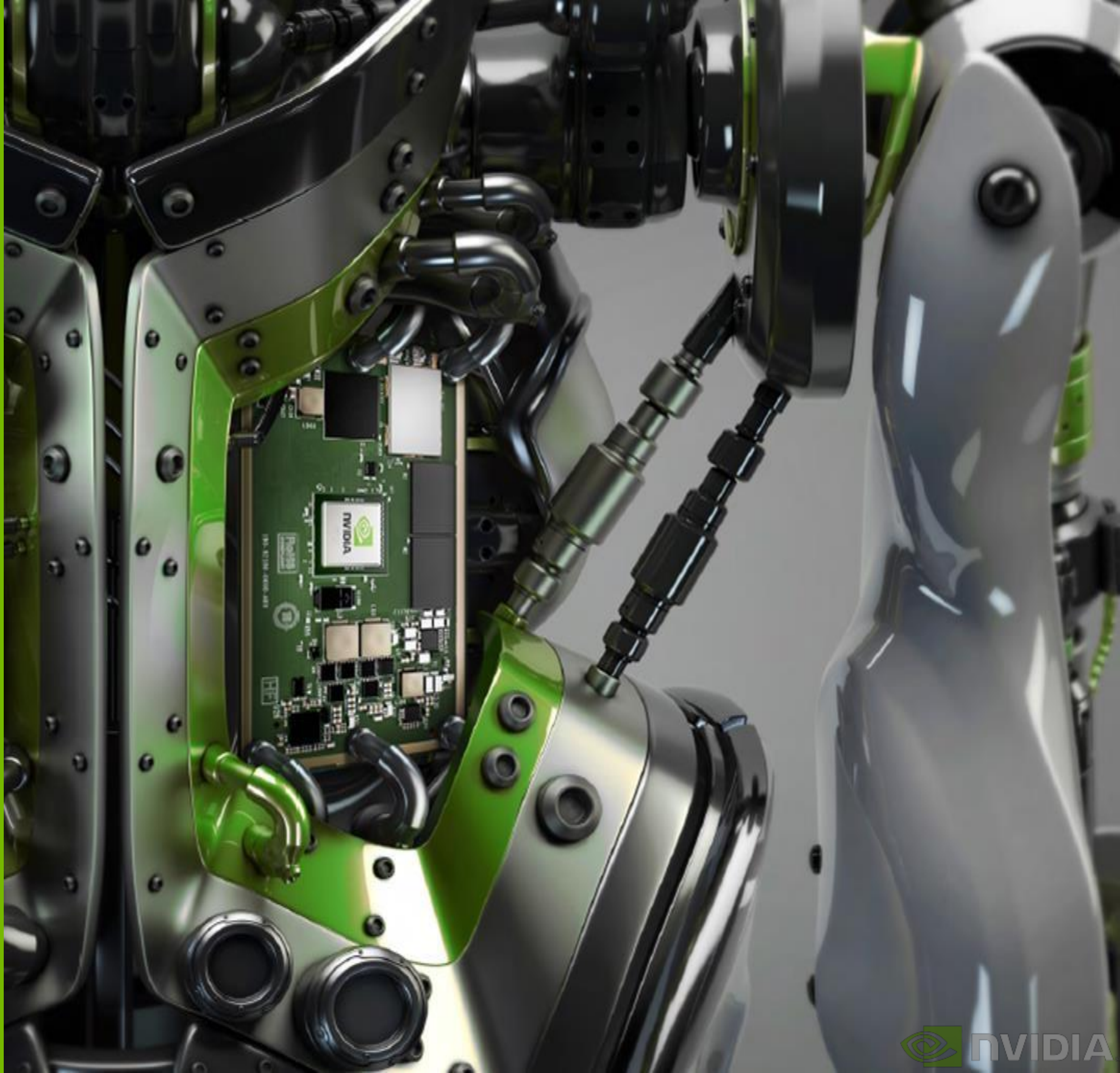


standard computer vision
features (e.g. HOG)
mid-level features (e.g. DPM)
Felzenszwalb '08
classifier (e.g. SVM)
deep learning
end-to-end training
tiger
tiger cat
jaguar
lynx
robotic control pipeline
observations
state estimation (e.g. vision)
modeling & prediction
planning
low-level control
controls
deep reinforcement learning
observations
end-to-end training
controls

Reinforcement Learning



arXiv:1611.06256 *GA3C: GPU-based A3C for Deep Reinforcement Learning*, Y. Kautz et al., NVIDIA Research, 2016.



REINFORCEMENT LEARNING

Reward function matters…

NVIDIA.

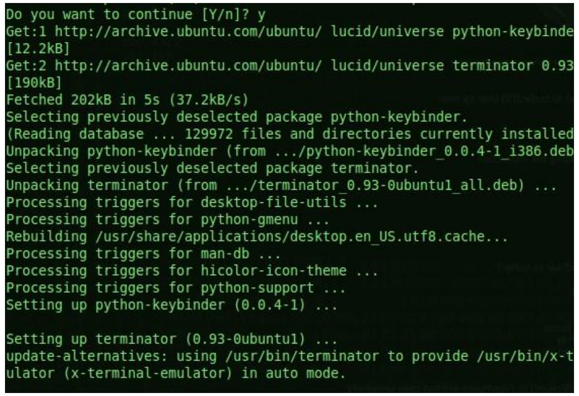
TWO DAYS TO A DEMO

Reinforcement Learning Edition

OpenAI Gym

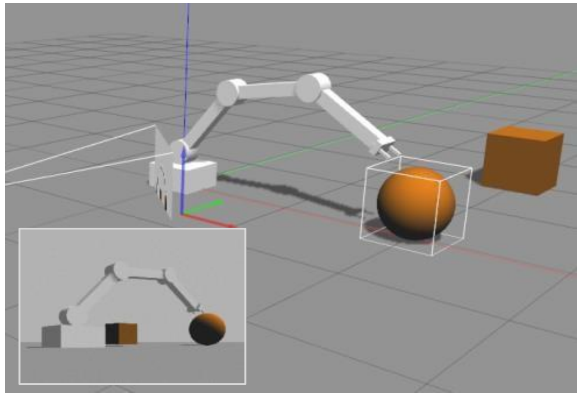
Test environments and games for
research and verification

RL Algorithms



DQN, DDPG, A3C, Actor Critic
PyTorch and TensorFlow

Robotic Simulation



Observation from vision
Pixels-to-actions

Transfer Learning

Adapt network to real robot
Online learning in the field

github.com/dusty-nv/jetson-reinforcement

NVIDIA

THANK YOU!

Q&A: WHAT CAN I HELP YOU BUILD?

2 Days To a Demo	github.com/dusty-nv/jetson-inference
Reinforcement Learning	github.com/dusty-nv/jetson-reinforcement
Access these Slides	github.com/dusty-nv/jetson-presentations

Post Discussion	devtalk.nvidia.com/default/topic/969035
eLinux TX2 Wiki	eLinux.org/Jetson_TX2

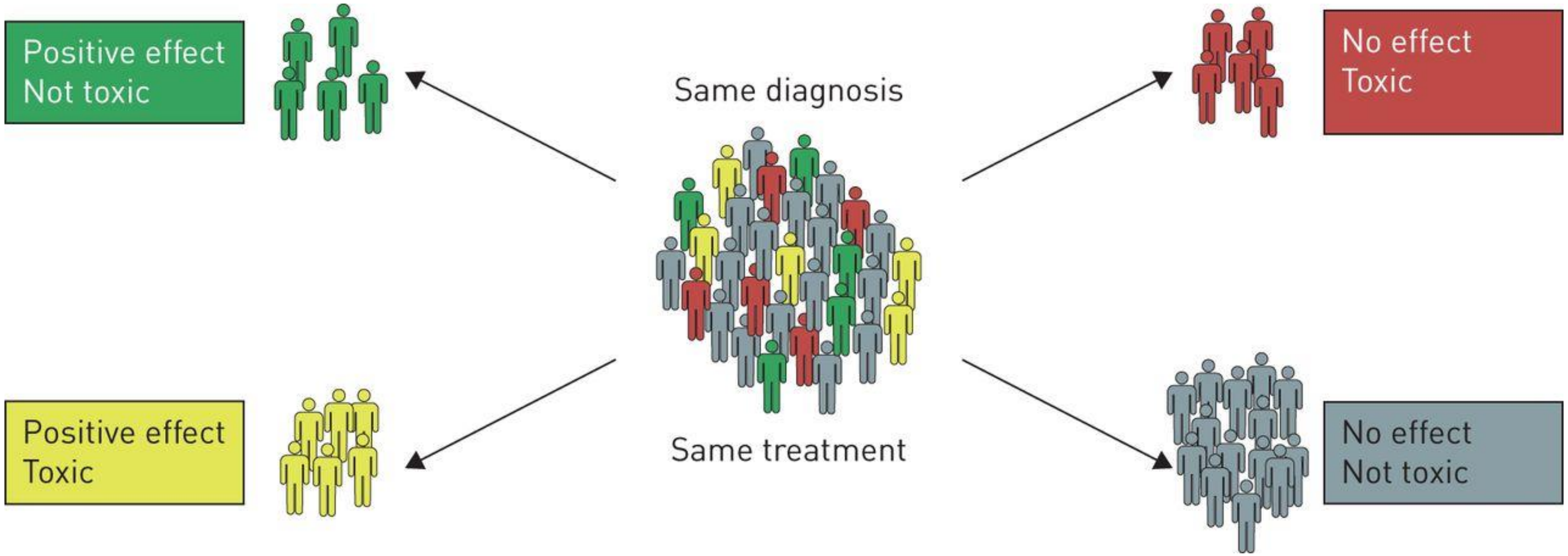
NVIDIA

DECODING GENOMICS

Discover possible, Solve intelligence

PRECISION MEDICINE

- The right drug, to the right disease at right time with right dose.
- NIH Precision Medicine Initiative and NCI Cancer Moonshot.



PRECISION MEDICINE IN ONCOLOGY

JOURNAL OF CLINICAL ONCOLOGY

Precision Oncology: An Overview

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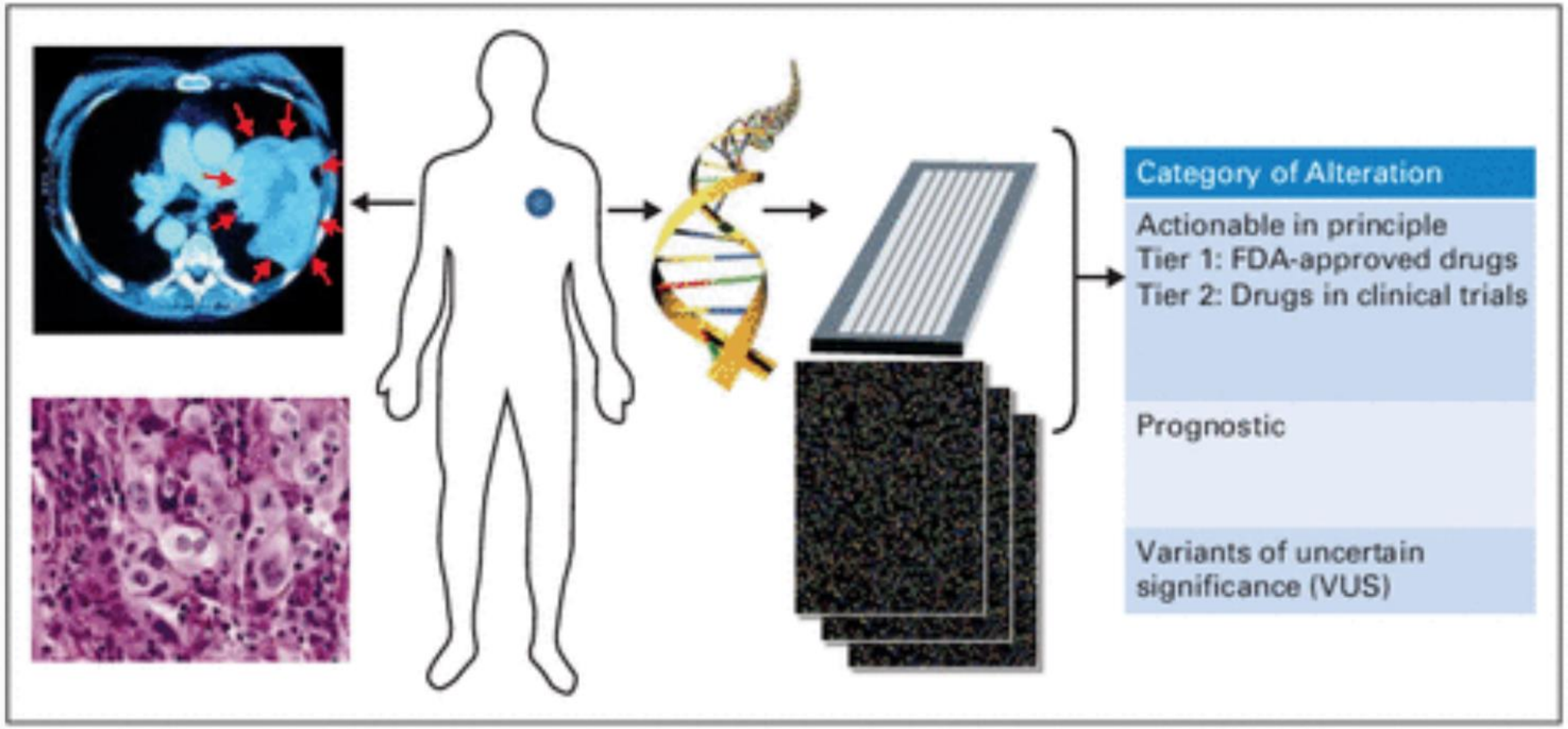
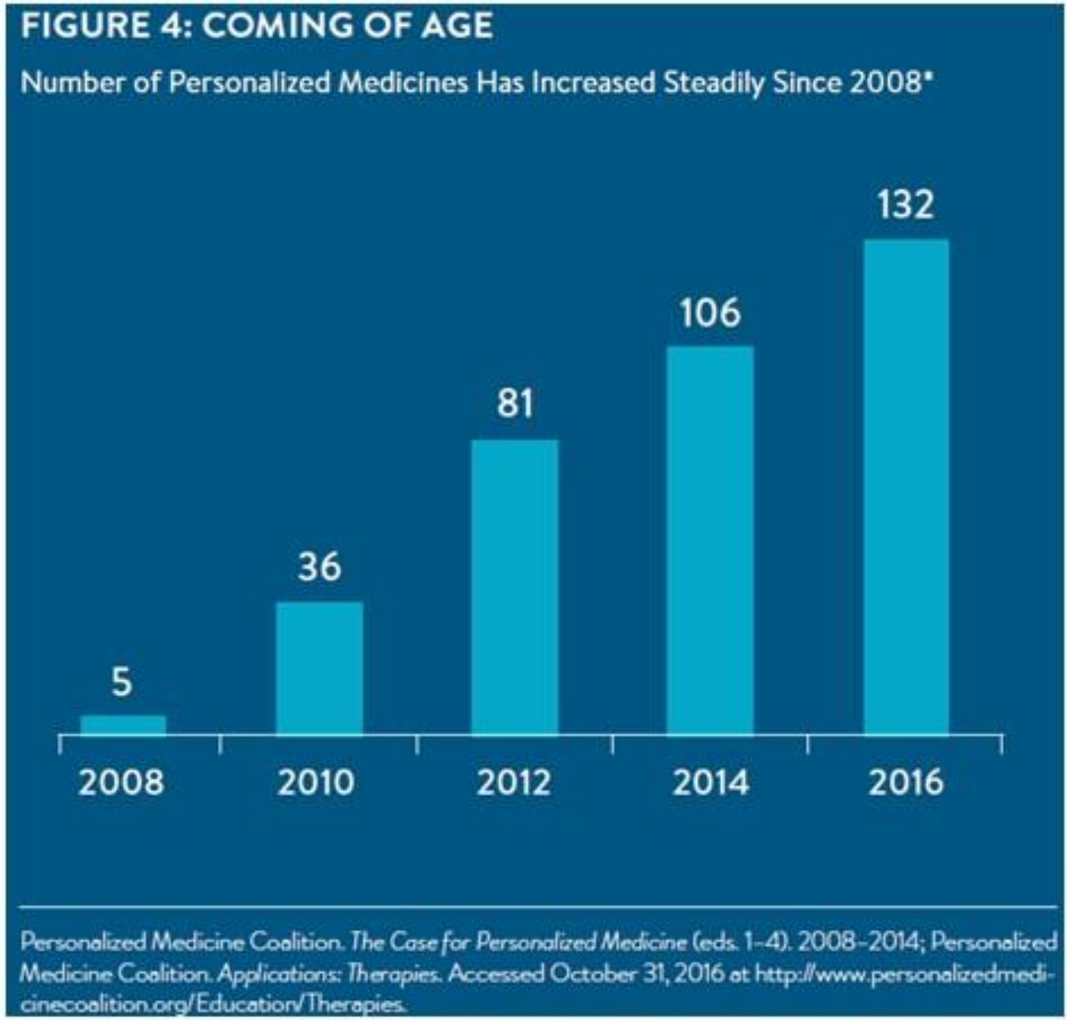
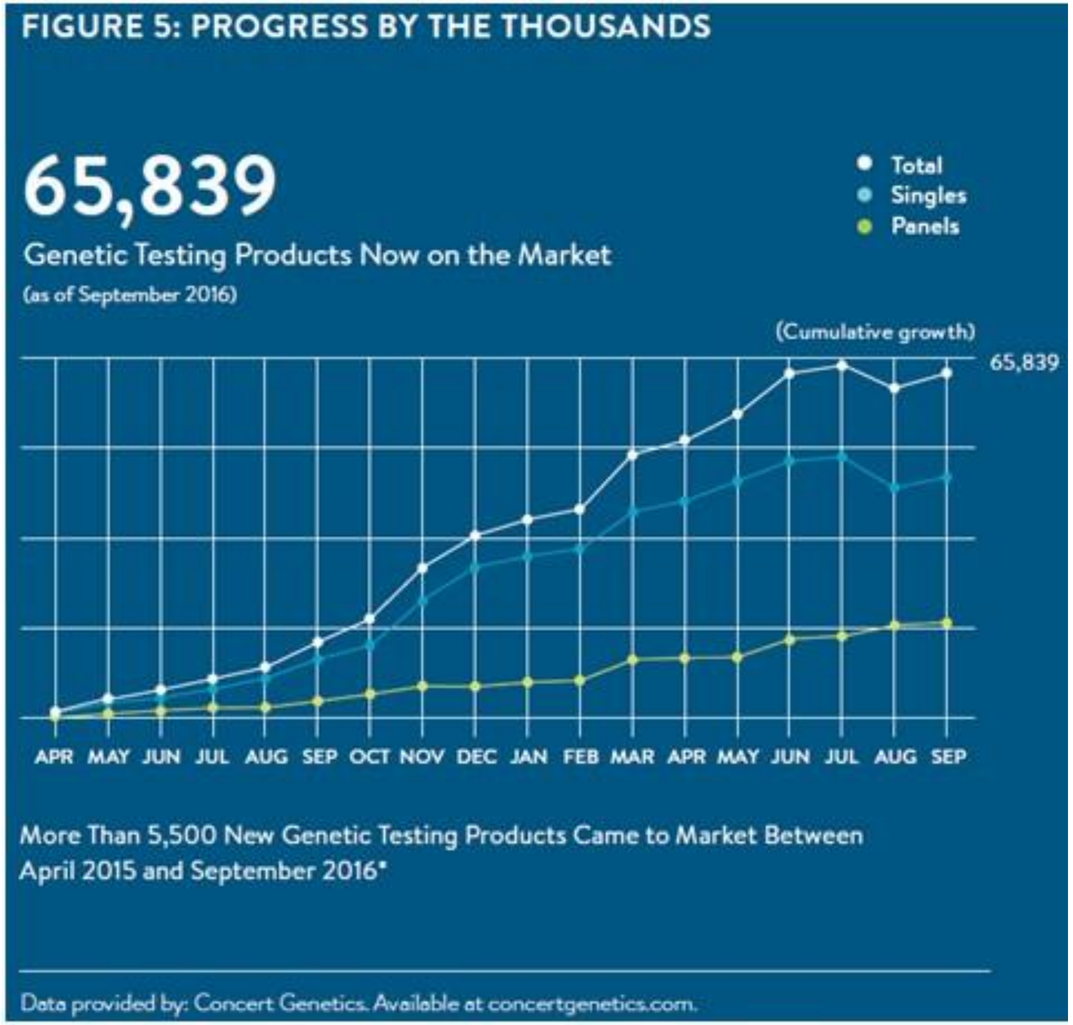


TRENDS



The Personalized Medicine Report 2017



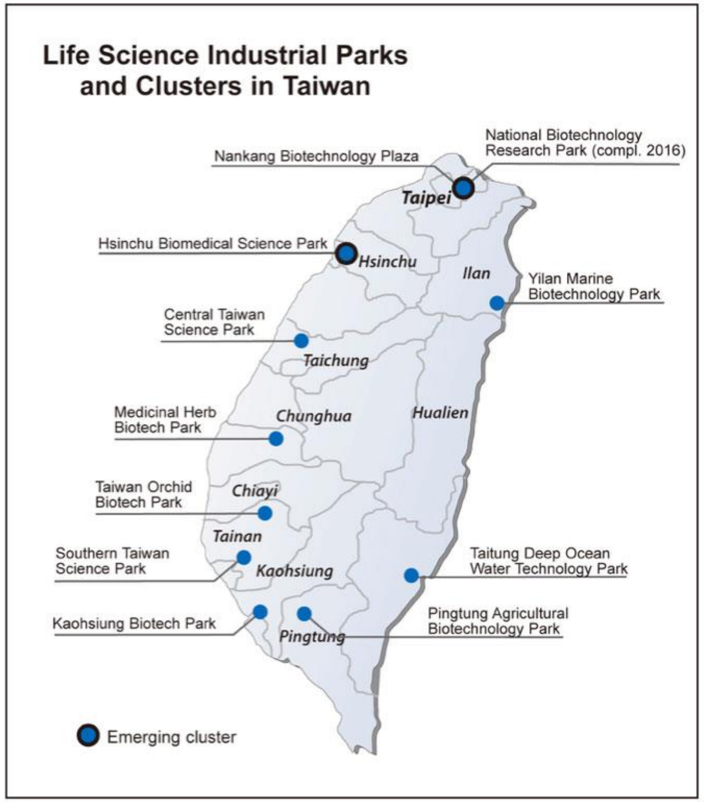
The Personalized Medicine Report 2017

THE 2016 *SCIENTIFIC AMERICAN WORLDVIEW* OVERALL SCORES

RANK		1.1	1.2	2.1	2.2	3.1	3.2	3.3	3.4	3.5	3.6	4.1	4.2	4.3	4.4	5.1	5.2	5.3	5.4	5.5	6.1	6.2	6.3	6.4	7.1	7.2	7.3	7.4	#1	#2	#3	#4	#5	#6	#7	SCORE
1	UNITED STATES	10.0	10.0	10.0	8.5	4.1	3.6	9.0	5.2	10.0	10.0	8.4	10.0	8.1	9.2	4.4	5.4			10.0	5.3	6.6	8.1	8.6	7.4	7.1	7.1	8.3	10.0	9.2	6.4	8.9	6.6	7.1	7.5	39.8
2	SINGAPORE			7.0	9.7				7.4	0.1		10.0		8.4	9.3			5.7	7.0	0.7	3.3	4.6	9.7	8.6	9.2	10.0	10.0	9.3		8.3	3.8	9.2	4.5	6.6	9.6	30.0
3	DENMARK	0.2	0.3	9.1	7.9	6.2	10.0	10.0	10.0	0.1	0.4	9.1	0.2	2.5	8.2	4.2	2.0	9.3		0.3	5.6	7.1	8.1	9.7	8.4	8.5	8.4	9.9	0.2	8.5	7.3	5.0	3.9	7.6	8.8	29.5
4	NEW ZEALAND	0.0	0.0	6.1	9.4				9.6	0.1		9.8		6.9	6.9	10.0	10.0	4.5		0.5	1.2	2.8	5.8	8.0	10.0	9.0	9.1	9.7	0.0	7.7	4.8	7.9	6.2	4.5	9.4	29.0
5	AUSTRALIA	0.5	1.4	6.8	8.5	8.0	4.6	5.2	7.0	0.9	0.0	7.8	0.3	3.8	8.4	7.0	5.8	5.3	5.3	3.4		5.2	5.6	8.5	8.8	7.7	8.9	9.4	1.0	7.6	5.1	5.0	5.3	6.4	8.7	28.0
6	SWITZERLAND	0.2	0.4	7.5	9.7	5.9	3.2	4.4	4.1	0.3	0.9	6.5	0.3	5.6	8.7	3.6	3.3	7.2		0.6	5.7	6.9	10.0	9.5	9.3	9.7	8.8	9.7	0.3	8.6	3.6	5.3	3.7	8.0	9.4	27.7
7	FINLAND	0.0	0.1	9.1	10.0	1.6	0.0	0.1	1.1	0.1	0.0	8.1	0.1	8.1	8.3	3.6	2.0	9.0		0.2	6.4	8.0	9.2	9.1	9.4	9.3	9.0	10.0	0.0	9.5	0.6	6.1	3.7	8.2	9.4	26.8
8	UNITED KINGDOM	0.6	0.8	8.5	9.1	1.6	0.8	3.4	4.1	1.4		8.5	0.8	6.3	9.3	7.6	6.4	5.1	2.3	5.8	2.8	3.7	6.7	9.1	6.9	7.8	8.8	9.2	0.7	8.8	2.2	6.2	5.4	5.6	8.2	26.5
9	SWEDEN	0.1	0.5	8.5	8.5	6.7	1.1	1.8	2.2	0.3	0.1	8.3	0.5	5.9	8.4	2.5	2.3	7.3		0.4	6.4	7.7	7.5	10.0	8.8	8.4	8.7	9.6	0.3	8.5	2.4	5.8	3.1	7.9	8.9	26.3
10	CANADA	0.0	0.9	9.1	8.5	3.5	0.2	0.1	3.3	0.8	0.1	7.8	1.0	5.6	10.0		6.4	5.3	4.5	1.6	2.1	3.9	6.9	8.2	9.1	8.3	8.8	9.2	0.5	8.8	1.6	6.1	4.4	5.3	8.9	25.3
11	HONG KONG	0.1	0.0	5.2	9.1	0.4	1.3	3.2	1.5			8.9		7.5	9.4			2.9		0.3		1.6	9.7	8.7	8.9	8.6	9.5	9.1	0.0	7.1	1.6	8.6	1.6	6.7	9.0	24.7
12	GERMANY	0.1	0.5	8.3	8.2	0.9	0.3	0.4	1.1	1.6	0.4	7.7	0.6	5.0	6.9	4.8	2.9	6.5	5.1	2.8	5.3	6.7	8.3	8.0	8.4	8.2	8.4	9.1	0.3	8.2	0.8	5.0	4.4	7.1	8.5	24.6
13	ISRAEL	0.0	0.6	6.6	6.1	10.0	1.1	0.2	6.3	0.1	0.1	4.9		8.1	6.5		4.2	10.0	3.6	0.0	10.0	10.0	3.9	6.2	2.7	6.0	6.9	6.6	0.3	6.3	3.5	6.5	4.5	7.5	5.6	24.4
14	NETHERLANDS	0.1	0.2	9.1	9.1	1.3	2.1	2.2	4.8	0.4	0.2	6.5	0.2	5.0	8.3	2.6	0.9	6.1		0.8	2.9	4.5	9.4	8.6	8.7	8.6	8.6	9.5	0.1	9.1	2.2	5.0	2.6	6.4	8.9	24.4
15	JAPAN	0.0	0.2	9.1	9.4	0.2	0.0	0.0	0.0	2.7	0.5	6.1	0.1	5.3	6.6	0.9		5.9	5.5	2.0	7.5	7.8	9.2	7.0	8.6	8.5	6.7	8.3	0.1	9.2	0.6	4.5	3.6	7.9	8.0	24.2
16	IRELAND	0.0	0.1	9.1	8.8	1.8	1.2	0.9	5.9	0.1	0.1	7.5	0.0	4.1	7.7	7.3	4.3	5.0		0.1	3.0	3.6	5.6	8.0	8.8	7.7	8.6	8.9	0.0	8.9	2.0	4.8	4.2	5.0	8.5	23.9
17	FRANCE	0.2	0.9	9.1	8.5	1.8	1.4	1.3	3.0	1.3	1.2	6.5	0.9	4.7	7.2	5.3	3.0	6.9	2.8	3.7	3.9	5.2	8.3	7.5	6.7	6.9	6.5	7.8	0.6	8.8	1.8	4.8	4.3	6.2	7.0	23.9
18	AUSTRIA	0.0	0.0	7.5	8.2	0.5	0.1	0.1	2.2	0.1	0.1	7.3	0.0	3.1	6.0	3.3	2.7	6.6		0.8	5.7	6.6	8.6	9.1	9.4	7.6	7.8	9.5	0.0	7.9	0.6	4.1	3.4	7.5	8.5	22.8
19	NORWAY	0.0	0.1	6.8	8.5	2.5	0.1	0.0	4.1	0.2	0.0	8.2	0.0	7.2	7.6	2.7	1.5	6.3		0.2	2.2	3.7	5.8	9.1	8.9	8.5	8.2	9.8	0.0	7.6	1.4	5.8	2.7	5.2	8.8	22.6
20	BELGIUM	0.0	0.2	9.1	8.2	2.3	0.7	0.5	7.0	0.2	0.2	5.5	0.2	5.0	6.8	2.4	1.4	6.2		0.6	4.3	5.2	6.9	6.9	7.7	6.9	6.8	8.0	0.1	8.6	2.2	4.4	2.6	5.8	7.4	22.2
21	LUXEMBOURG			6.7	10.0							4.2	0.0	7.5			0.6	8.7			1.8	2.6	7.5	9.0	9.7	7.9	8.2	9.3		8.3		3.9	4.6	5.2	8.8	22.0
22	ICELAND			3.8	7.0							7.4		3.8		4.1	4.7	7.9		0.0	2.8	5.8	8.6	9.1	9.3	7.3	6.9	8.7		5.4		5.6	4.2	6.6	8.0	21.3
23	TAIWAN, CHINA	0.0	0.1	4.9	6.7	0.4	0.0	0.0	0.0	0.2		7.9		6.9	6.2				2.6		6.4		7.2	7.1	8.0	6.8	7.2	6.9	0.0	5.8	0.1	7.0	2.6	6.9	7.2	21.1
24	SOUTH KOREA			7.5	3.6				0.7	0.5	0.5	8.9	0.1	2.2	8.1	4.4	3.7	6.8	3.7	0.8	9.3	9.5	7.5	7.0	6.2	6.0	6.6	6.2		5.6	0.6	4.8	3.9	8.3	6.3	21.0
25	ESTONIA				6.7						0.0	7.6		5.0	7.0	4.5	2.8	4.0		0.0	2.1	5.0	5.8	6.4	7.9	5.5	8.3	7.5		6.7		6.5	2.8	4.8	7.3	20.1
26	UAE				7.6					0.1		6.3		7.8	6.7			0.7		0.7		1.0	9.7	6.2	8.0	7.2	6.2	5.3		7.6	0.1	6.9	0.7	5.6	6.7	19.7
27	MALAYSIA			3.7	7.3				2.2	0.1		7.5		9.1	7.3	3.3		2.1		0.8		2.5	7.5	4.6	6.6	5.9	5.8	5.1		5.5	1.1	8.0	2.1	4.9	5.9	19.6
28	QATAR				8.8					0.0		3.5		10.0		0.0				0.1		1.0	7.5		8.6	5.3	5.0	6.3		8.8	0.0	6.7	0.0	4.2	6.3	18.6
29	SPAIN	0.0	0.0	7.5	3.0				5.9	0.6	0.3	6.2	0.2	2.5	6.6	3.2	2.5	5.0	3.9	0.7	1.6	2.9	7.8	5.7	6.6	6.0	5.6	6.1	0.0	5.3	3.2	3.9	3.1	4.5	6.0	18.6
30	CZECH REPUBLIC			7.5	4.8				0.7	0.0	0.0	5.9	0.0	4.4	4.4	4.6	3.0	5.2		0.5	2.7	4.1	5.6	6.2	8.5	5.5	6.4	6.7	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

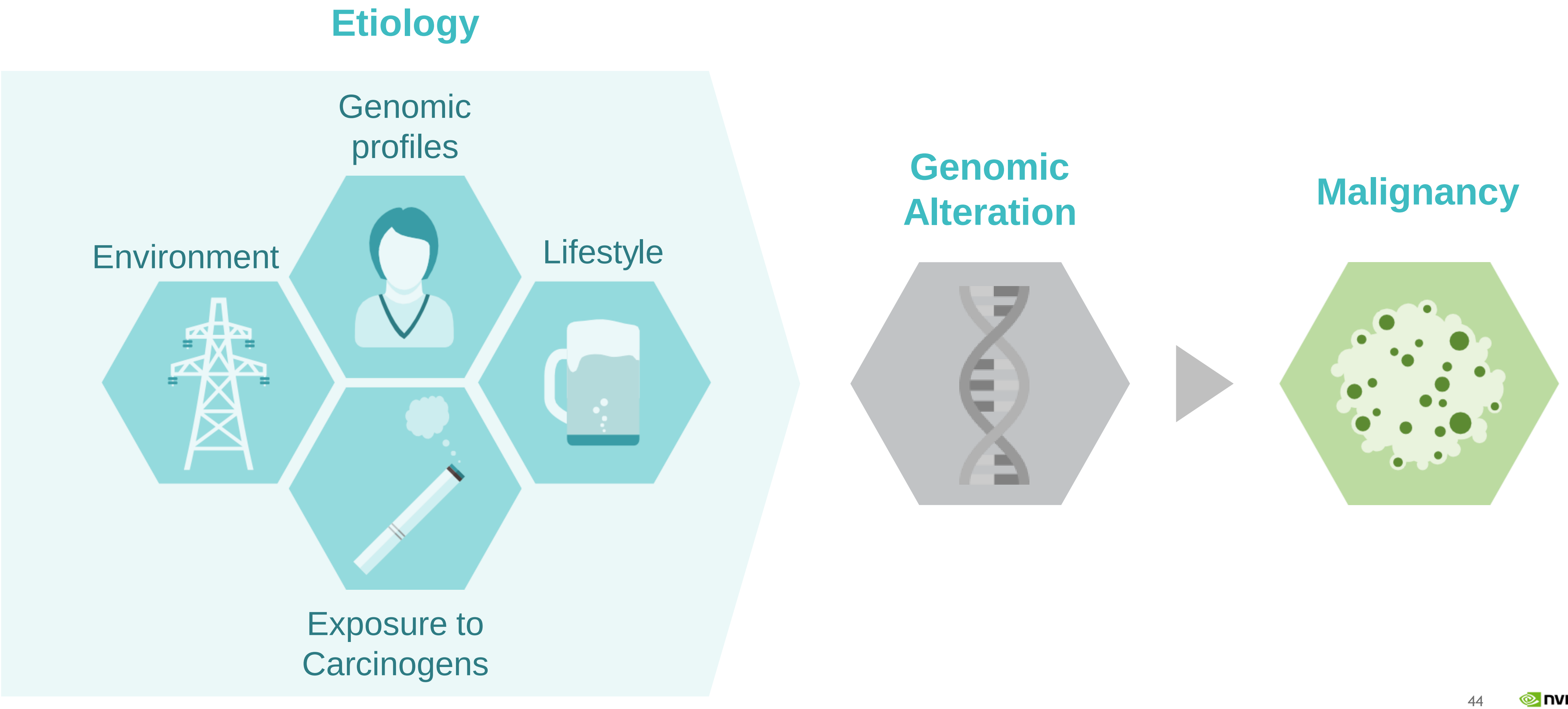
STRENGTH OF BIOTECH DEVELOPMENT IN TAIWAN

- Industrialized and competitive R&D activities
- Outstanding health care quality and National Health Insurance
- Competitiveness of Taiwan Clinical Trails in East Asia
- Clinical Trail Consortium & Central IRB Review System
- National Reference Lab & Biobank for Precision Medicine
- National efforts to promote biotechnology development



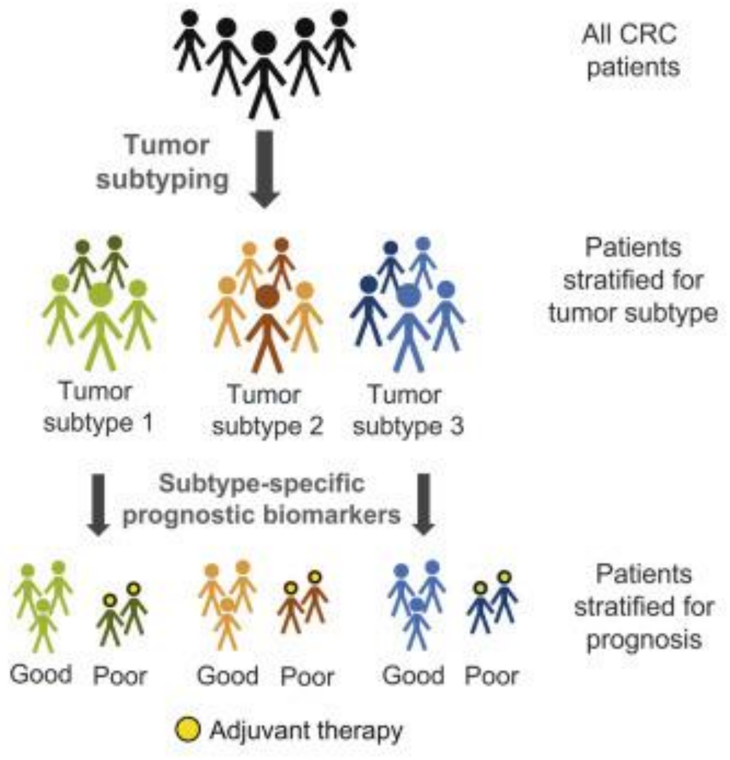
CANCER IS A DISEASE OF THE GENOME

Our understanding of cancer has been evolving

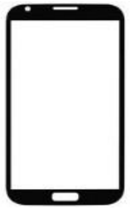


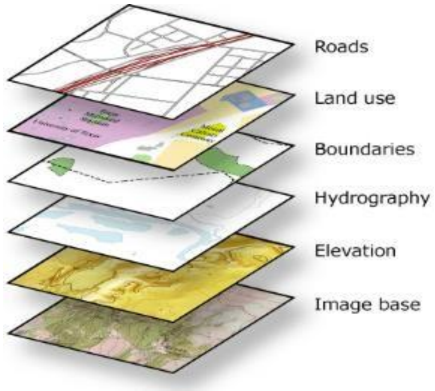
REMARKABLE BIOMARKER LANDSCAPE

- Rapid expanding …
- Established biomarkers
    - ALK (NSCLC)
    - ROS1 (NSCLC)
    - EGFR (NSCLC, CRC, MABC)
    - HER2 (BC)
    - KRAS (mCRC, NSCLC, *)
    - BRCA1 (BC, OC)
    - ….



WHAT HAPPEN IN PRECISION MEDICINE CLINIC





Classic

- IHC
- FISH
- PCR

Comprehensive molecular profiling

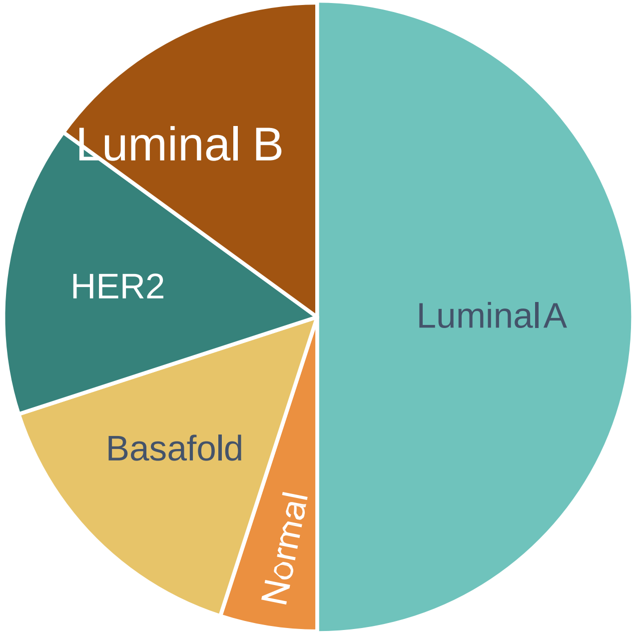
- Next-Generation DNA sequencing
- Protein analysis
- Immune signature analysis
- Liquid biopsy (cancer DNA detection from blood)

“MATCH” the therapy based on the profiling
Personalized/Precision Medicine approach

Adapted from Toward precision medicine, NAS 2013.

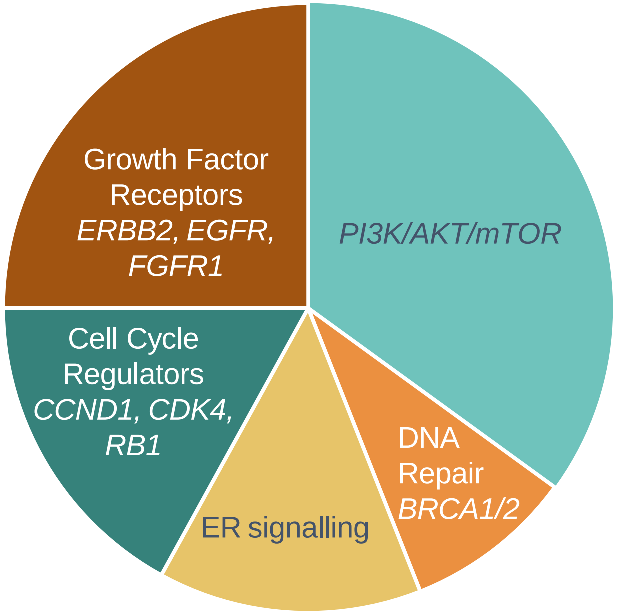
THE CLASSICAL APPROACH TO CANCER IS EVOLVING

2000: Breast cancer subtypes



Clinical decisions based on **affected tissue, histology** and **disease stage**

2017: Genomic drivers

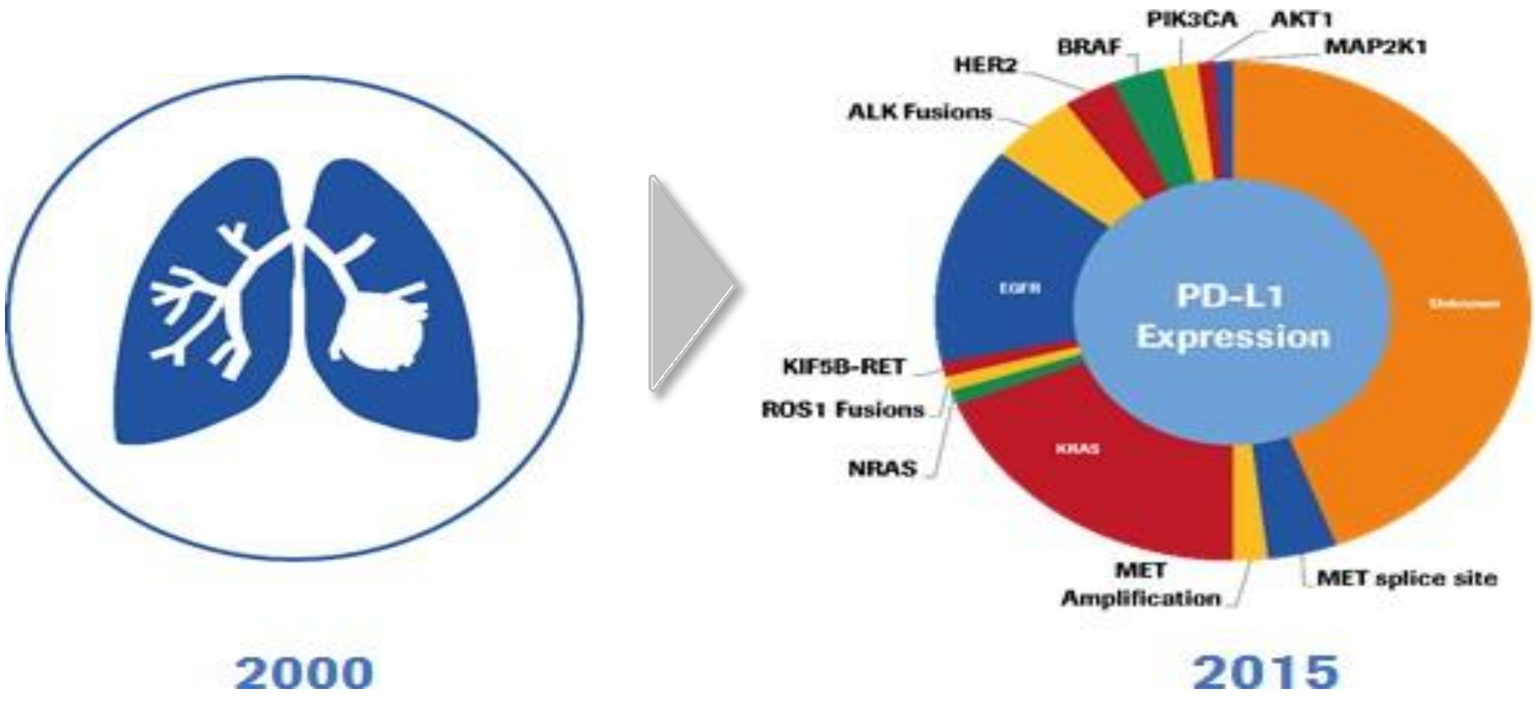


Clinical decisions based on the **results of comprehensive genomic profiling**

Adapted from: Ross, J. and Gay, L. (2016) *Pathology.* 49:120-32.

LUNG ADENOCARCINOMA

Moving from one disease to multiple disease types by molecular *alterations that require distinct tx plans*



Biomarker	Drugs
EGFR mutations	erlotinib, gefitinib, afatinib
ALK rearrangements	crizotinib
BRAF V600E	vemurafenib*, dafrafenib*
MET amplifications	crizotinib
ROS1 rearrangements	crizotinib
HER2 mutations	trastuzumab*, afatinib
RET rearrangements	cabozantinib*

** Drugs not approved for lung cancer*

PROFILING INITIATIVES

Investigating the potential to match treatments to genomics

CAPTUR Canadian Profiling and targeted Utilization trial

DRUP The Drug Rediscovery Protocol

TAPUR Targeted Agent and Profiling Utilization Registry Study

And more…

Initiatives to decipher which patients respond to which therapies, irrespective of in which tumor type the therapies are approved in

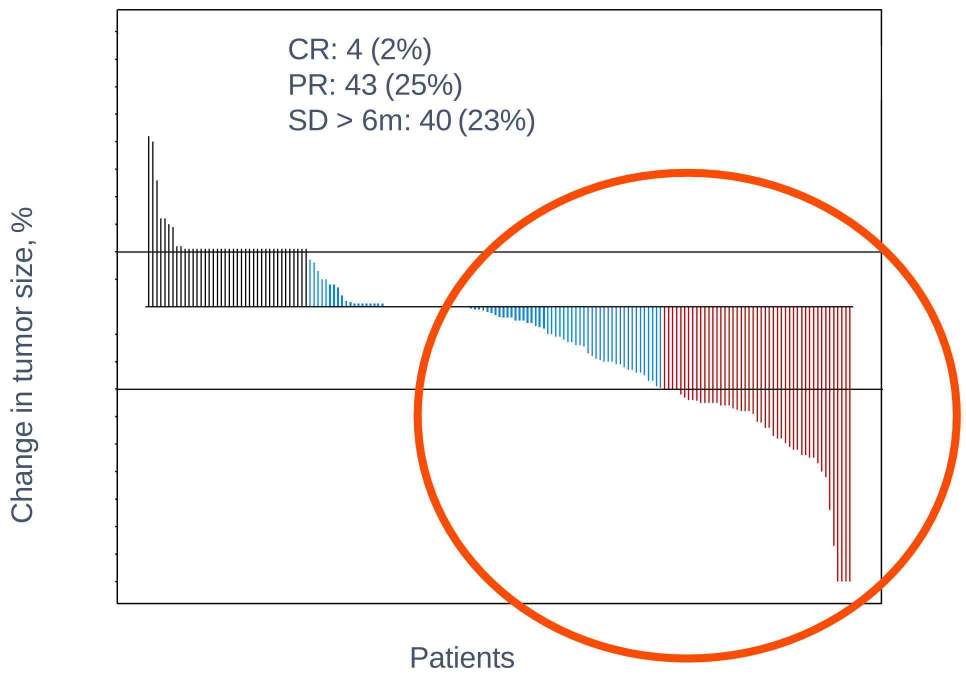
http://www.nature.com/nm/journal/v22/n5/fig_tab/nm.4089_T1.html

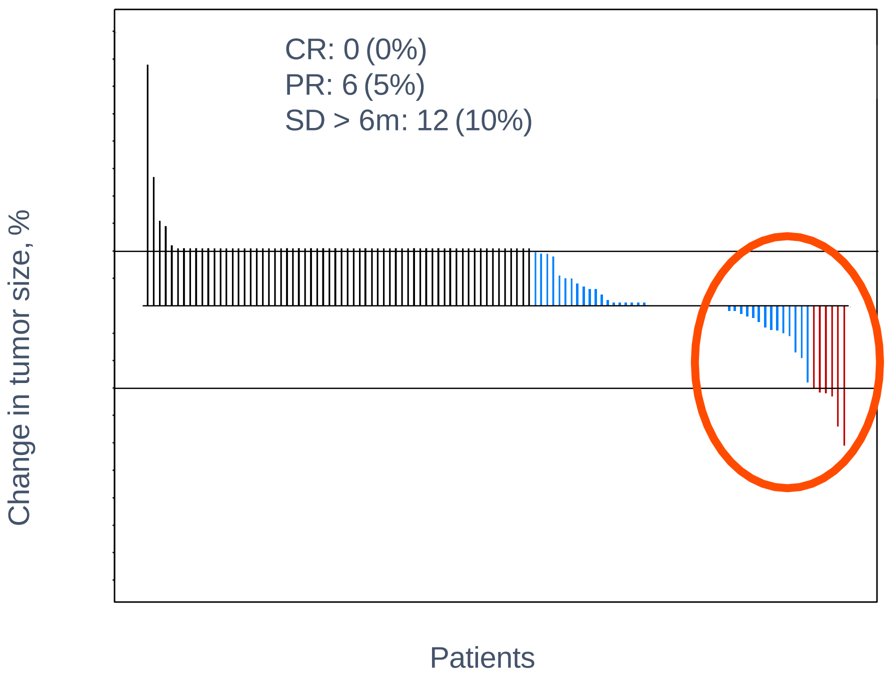
MATCHING PATIENTS WITH TARGETED DRUGS INCREASES RESPONSE RATES

Matched therapy
N = 175
Complete/Partial Response = 27%

P < .0001

Therapy without matching
N = 116
Complete/Partial Response = 5%



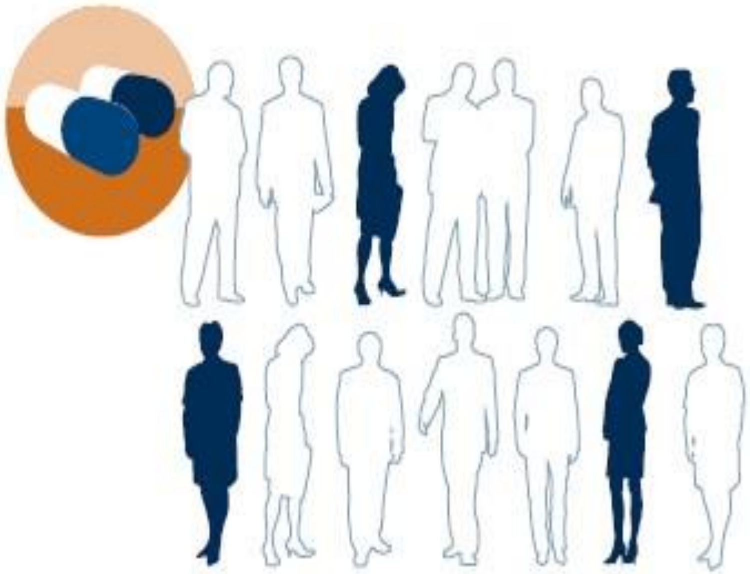


Janku, F., et al. (2011) *Mol Cancer Ther.* 10(3):558-65; Tsimberidou, A-M., et al. (2012) *Clin Cancer Res.* 18(22):6373-83; Janku, F., et al. (2012) *J Clin Oncol.* 30(4_suppl):459; Janku, F., et al. (2014) *Cell Rep.* 6(2):377–87.

REDESIGNING CANCER TRIALS: STAGE 1

Smaller Trials, Bigger Chance for Success

OLD MODEL: Large numbers of patients, not selected by molecular characteristics; lower chance of demonstrating effectiveness, since many participants do not have the molecular defects being targeted

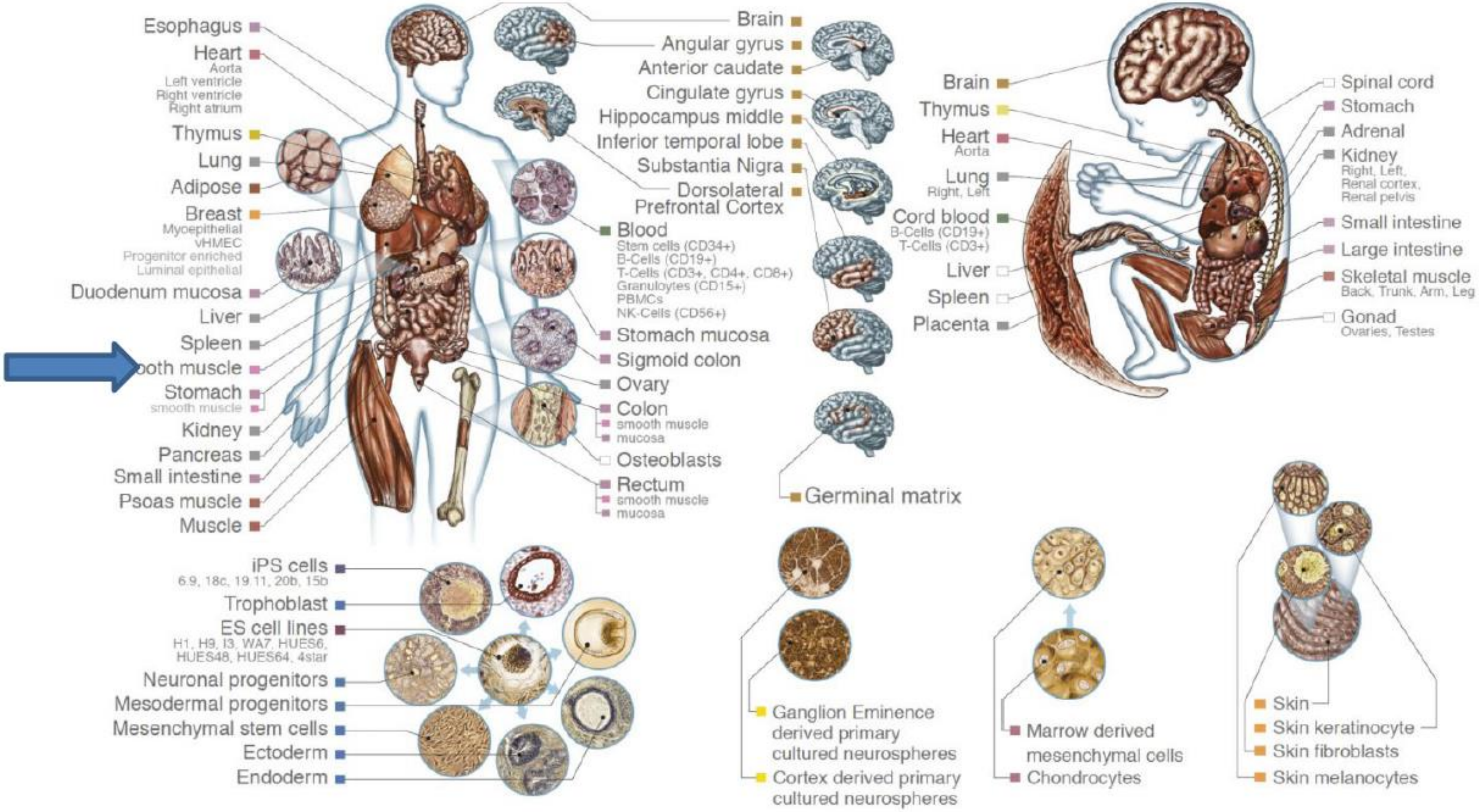


NEW MODEL: Small patient populations, all with the relevant mutations or genetic defects; greater chance of desired results, since all participants have the potential to respond

Tajik, P., et al. (2013) *Clin Cancer Res.* 19(17):4578-88.

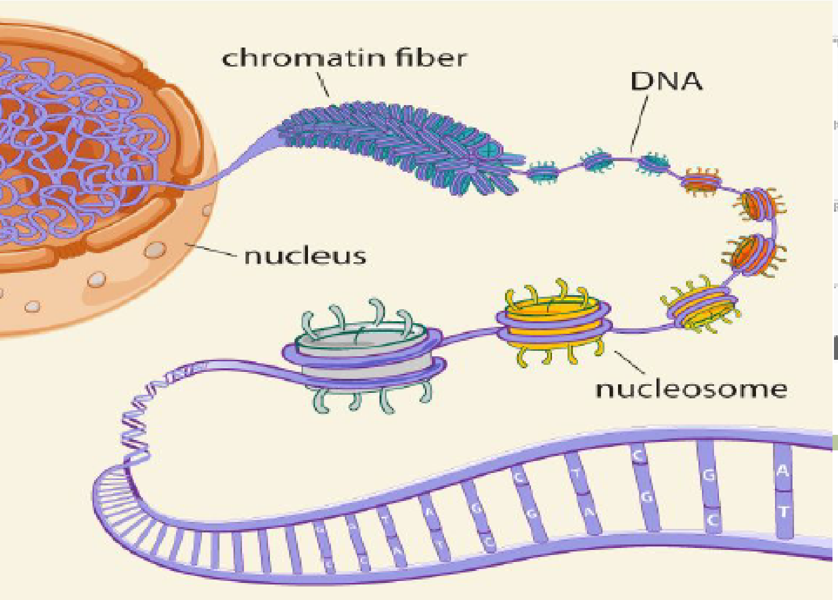
One genome ⇔ many cell types

ACCAGTTACGACGG
TCAGGGTACTGATA
CCCCAAACCGTTGA
CCGCATTTACAGAC
GGGGTTTGGGTTTT
GCCCCACACAGGTA
CGTTAGCTACTGGT
TTAGCAATTTACCG
TTACAACGTTTACA
GGGTTACGGTTGGG
ATTTGAAAAAAAGT
TTGAGTTGGTTTTT
TCACGGTAGAACGT
ACCTTACAAA............

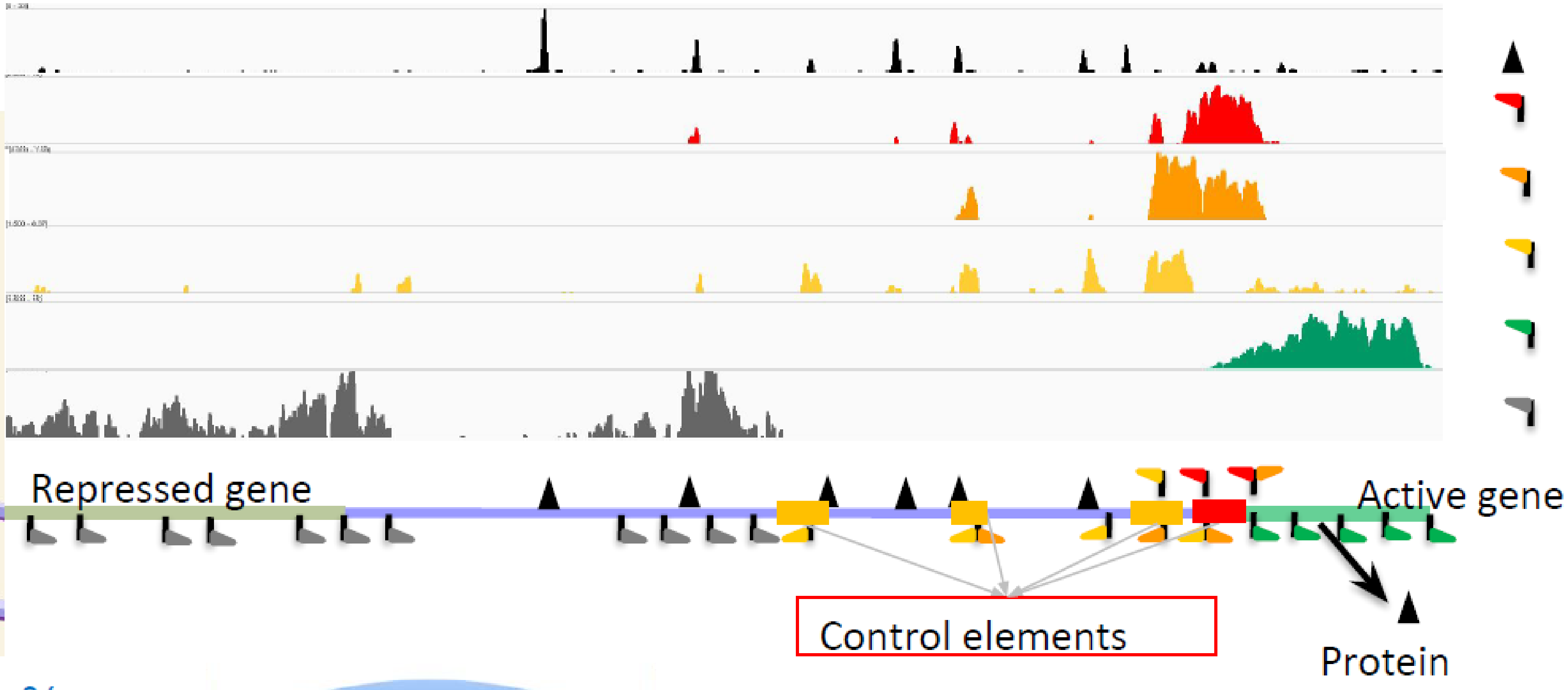


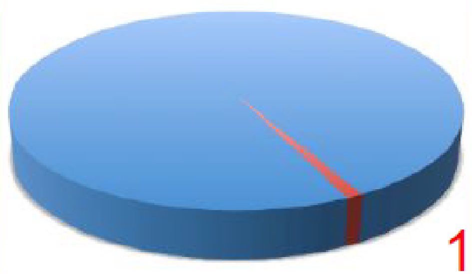
http://www.roadmapepigenomics.org/

Biochemical markers of functional elements

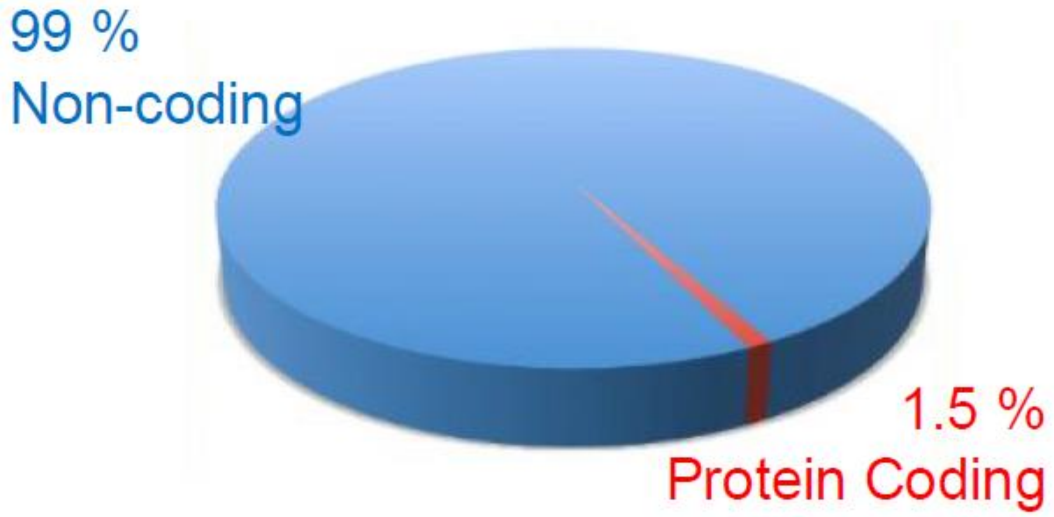


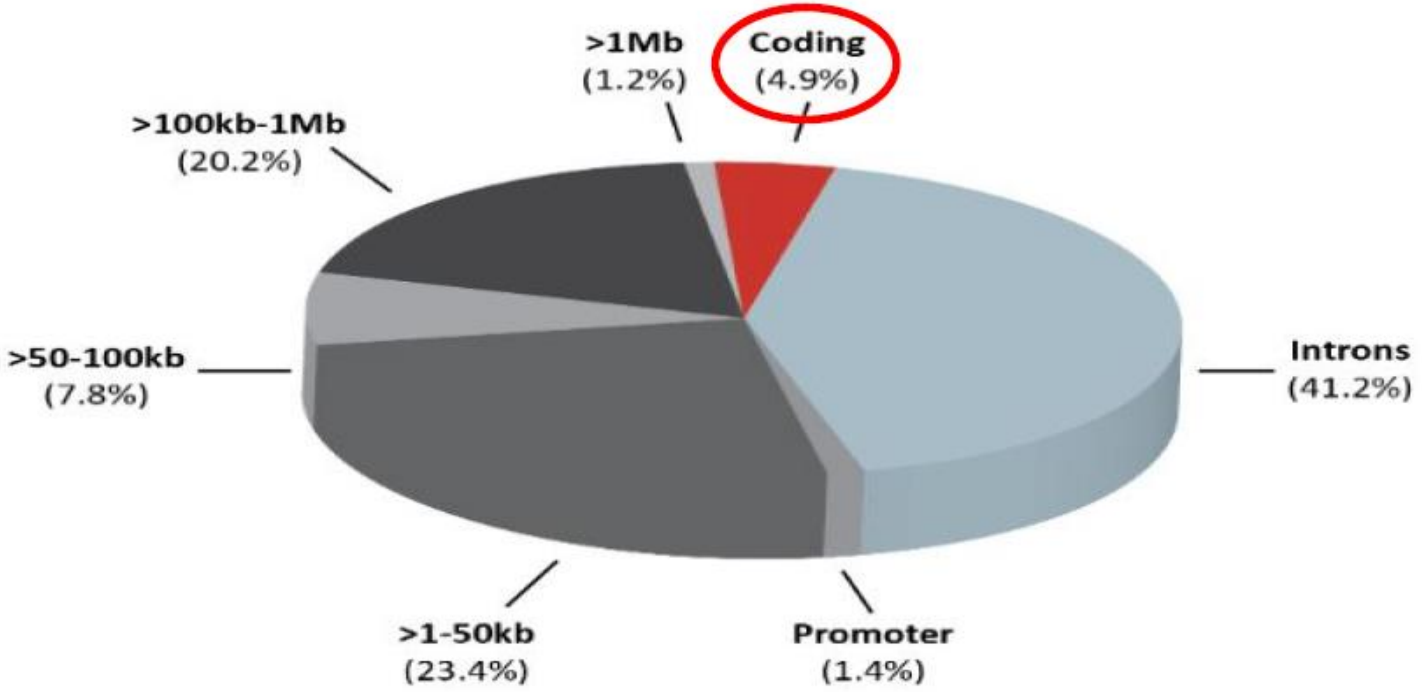
https://www.broadinstitute.org/news/1504





Why are control elements relevant in disease?

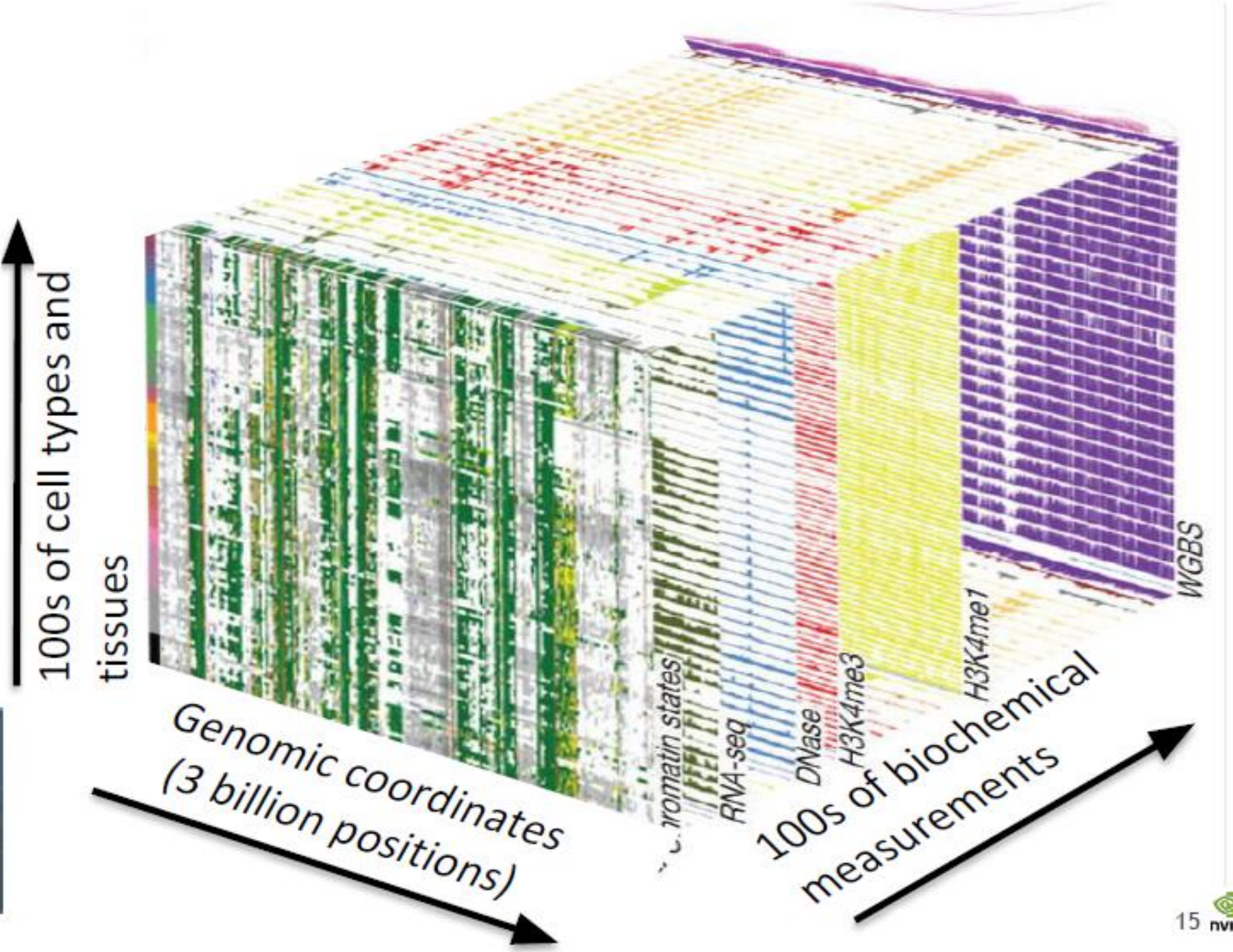




>90% of genetic variants associated with complex diseases do not disrupt protein-coding genes! Instead disrupting control elements!

Large-scale functional genomic data

- <u>**“Functional Genomics”**</u>
  Application of sequencing technology for **profiling 100s of biochemical markers of function** across the entire genome in 100s of different cell types and tissues



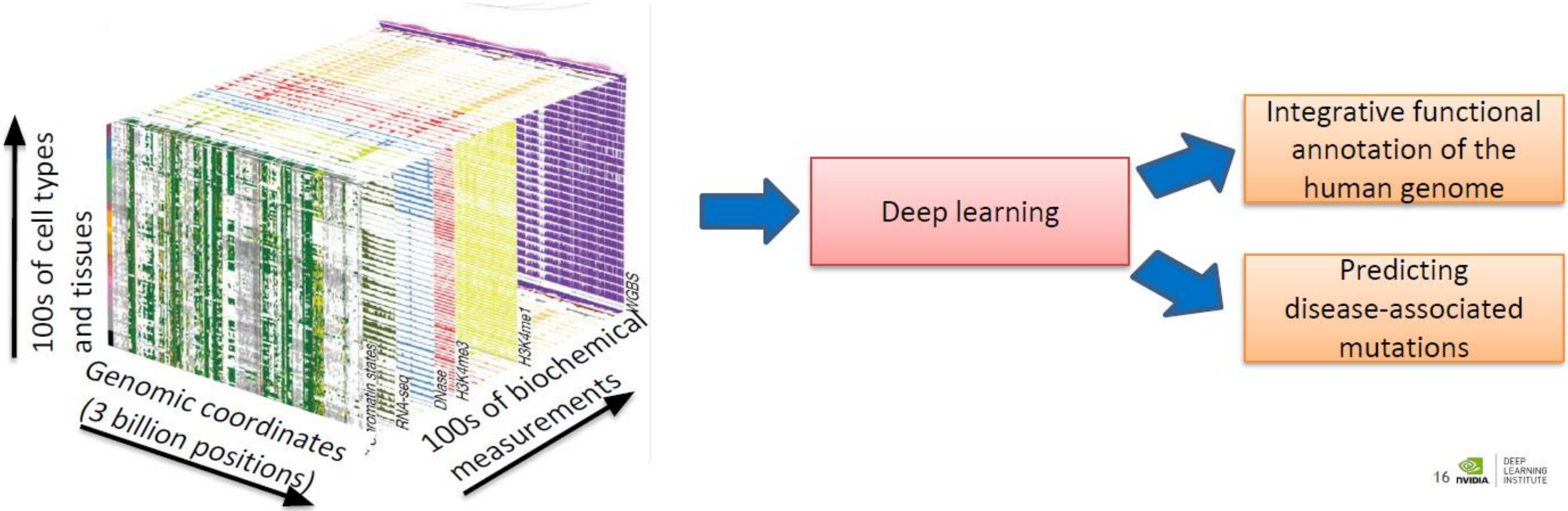
NIH funded collaborative consortia

ENCODE

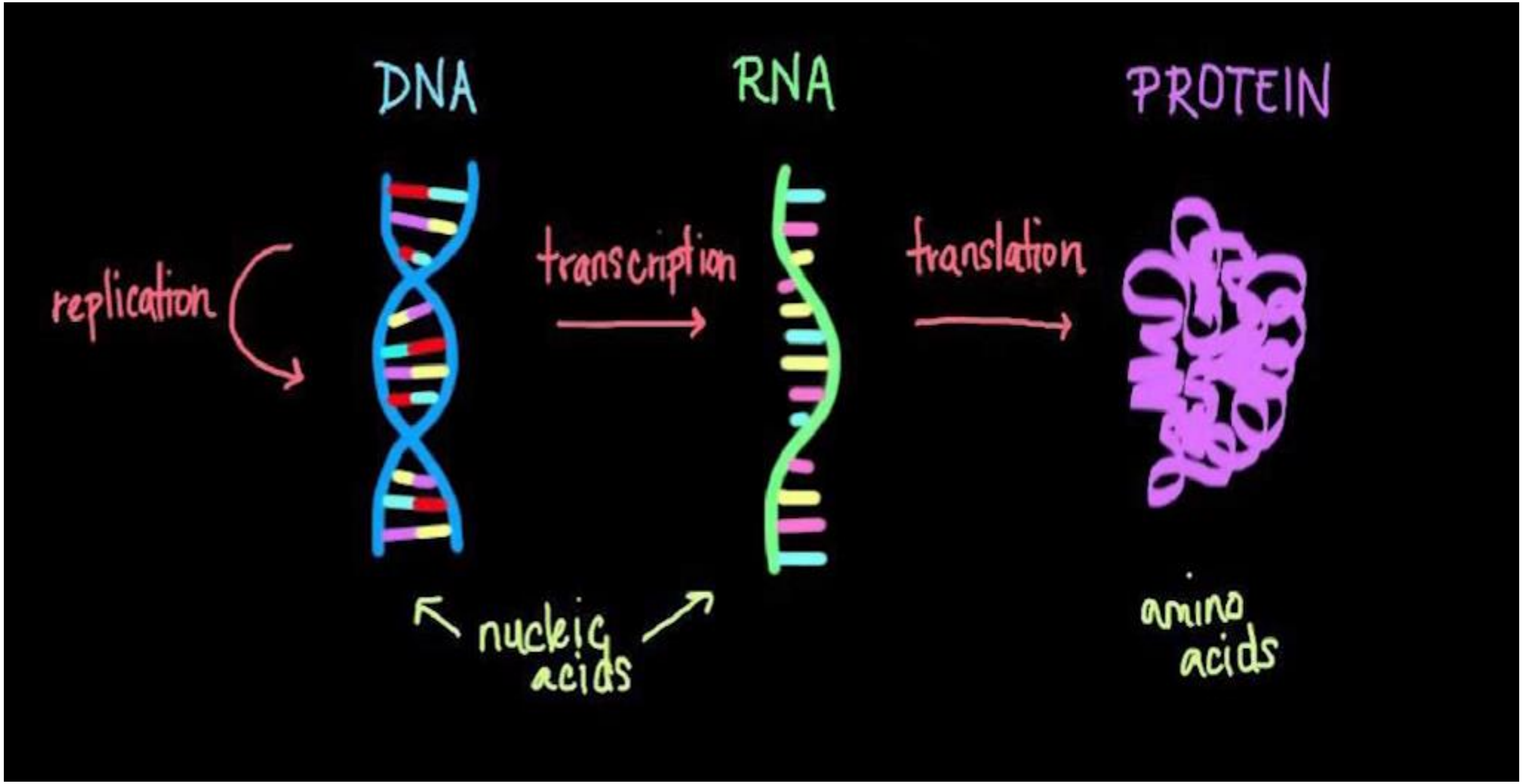
ROADMAP epigenomics PROJECT

Why deep learning and functional genomics?

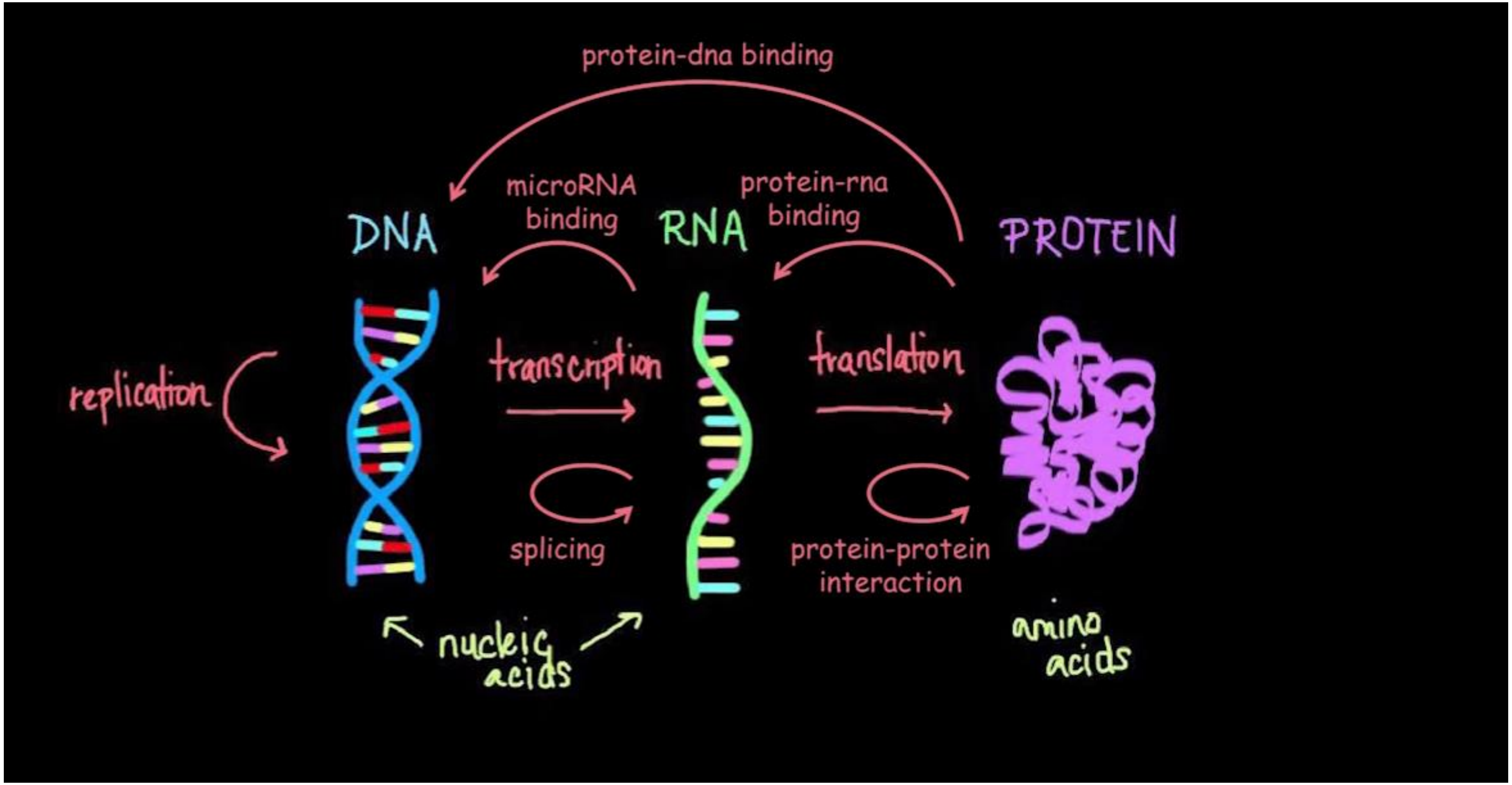
- **<u>Terascale data cube</u>** is rich and complex - deep learning is poised to integrate the heterogeneous data to decode genome function and its role in disease



CENTRAL DOGMA

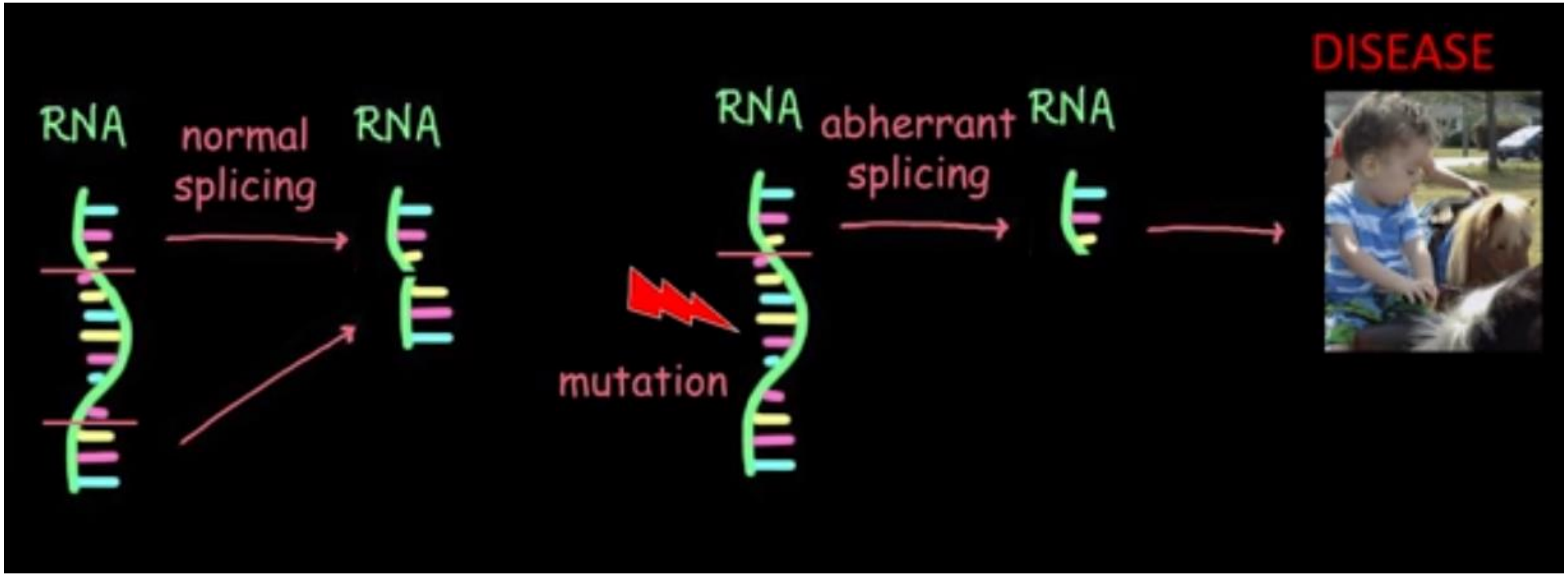


MORE COMPLEX



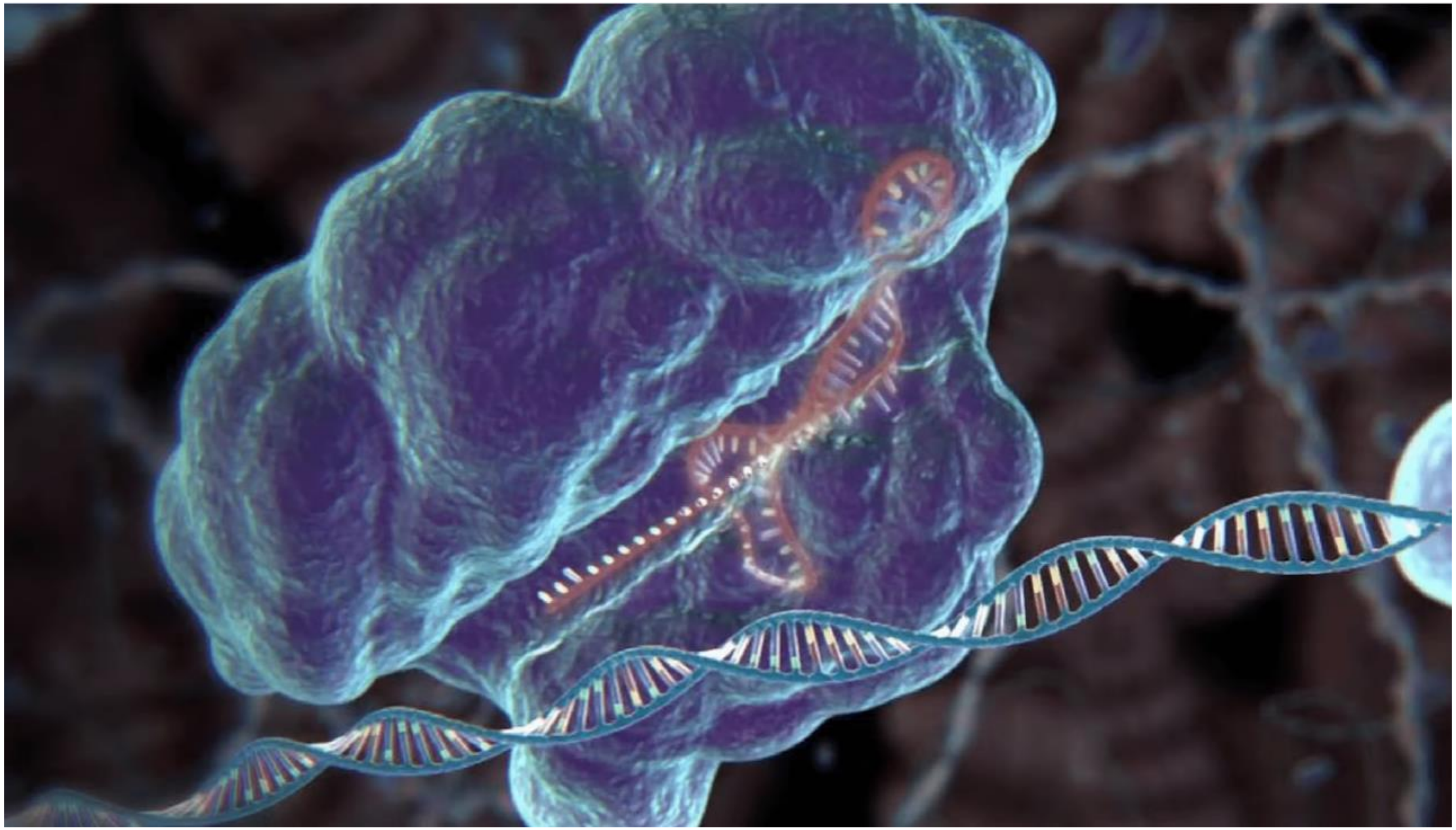
GENETIC DISEASE

Splicing goes wrong in spinal muscular atrophy

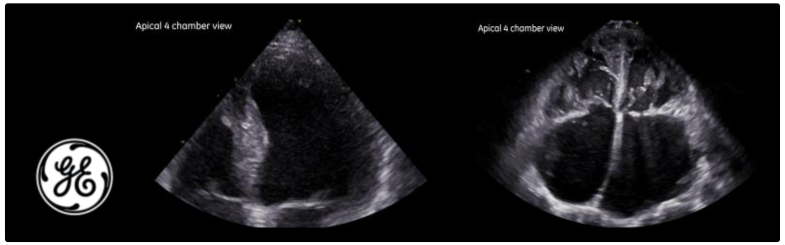


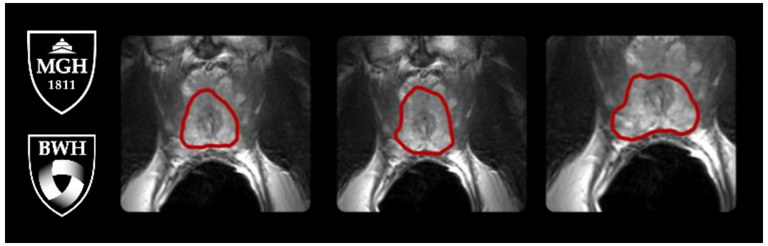
CRISPR CAS9

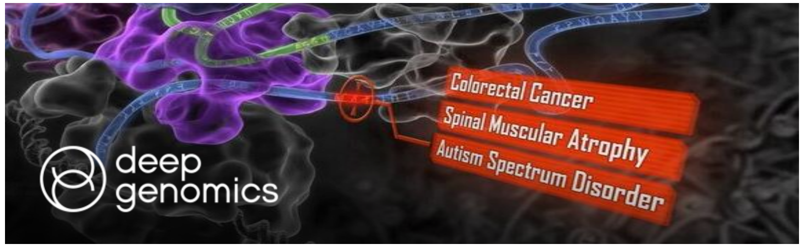
Edit DNA within living cells



DEEP LEARNING IS REVOLUTIONIZING HEALTHCARE







DETECT

DIAGNOSE

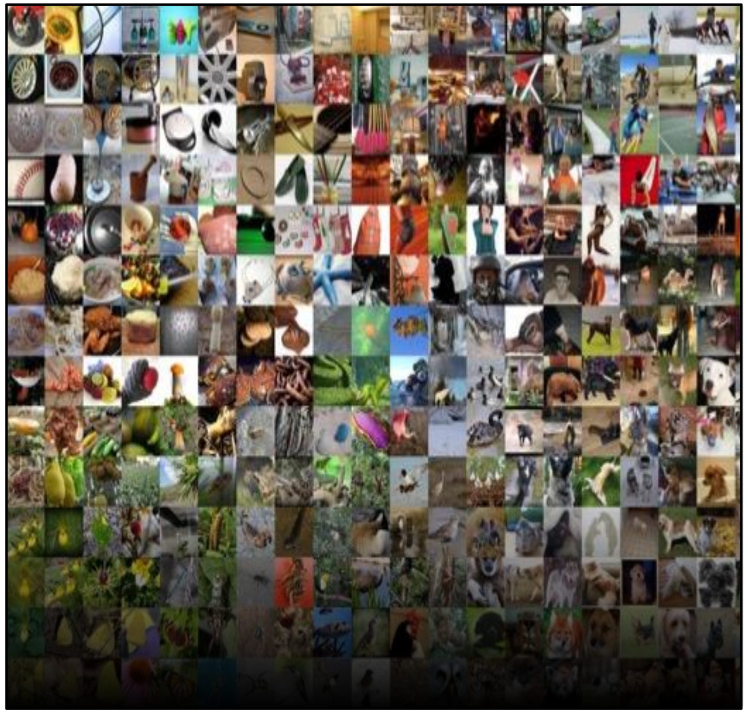
TREAT

zebra MEDICAL.VISION
BAYLABS
imagia
Genetesis SCIENCE MADE PERSONAL
SIG TUPLE
CLOUD MEDX

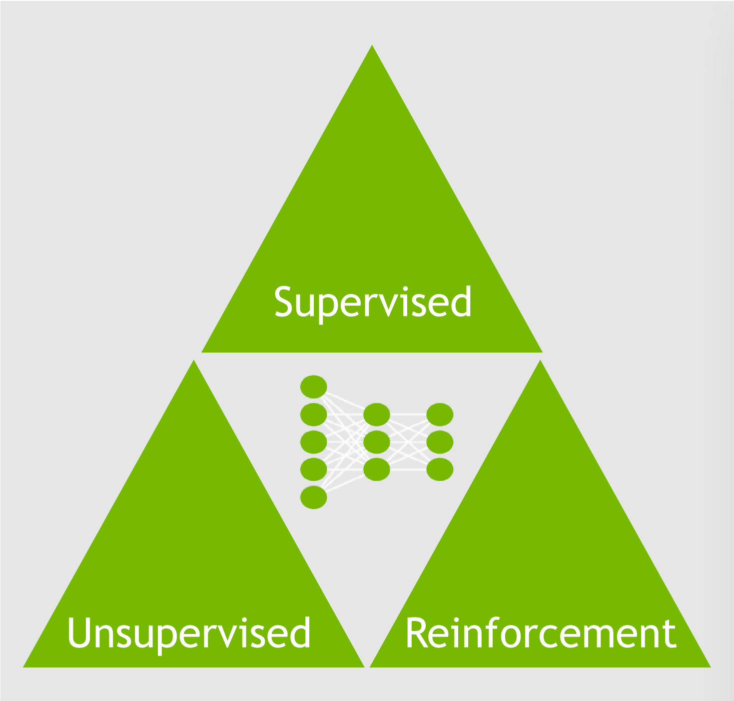
PHILIPS
MAYO CLINIC
Stanford MEDICINE
Paige.AI
ARTERYS
NIH

gsk
Celgene
PHENOMIC AI BIOIMAGE INFORMATICS
babylon
iCarbonX
lumiata

THE DEEP LEARNING RECIPE



Data



Algorithms

Compute

A NEW COMPUTING MODEL

Algorithms that Learn from Examples

Traditional Approach

- Requires domain experts
- Time consuming
- Error prone
- Not scalable to new problems

A NEW COMPUTING MODEL

Algorithms that Learn from Examples

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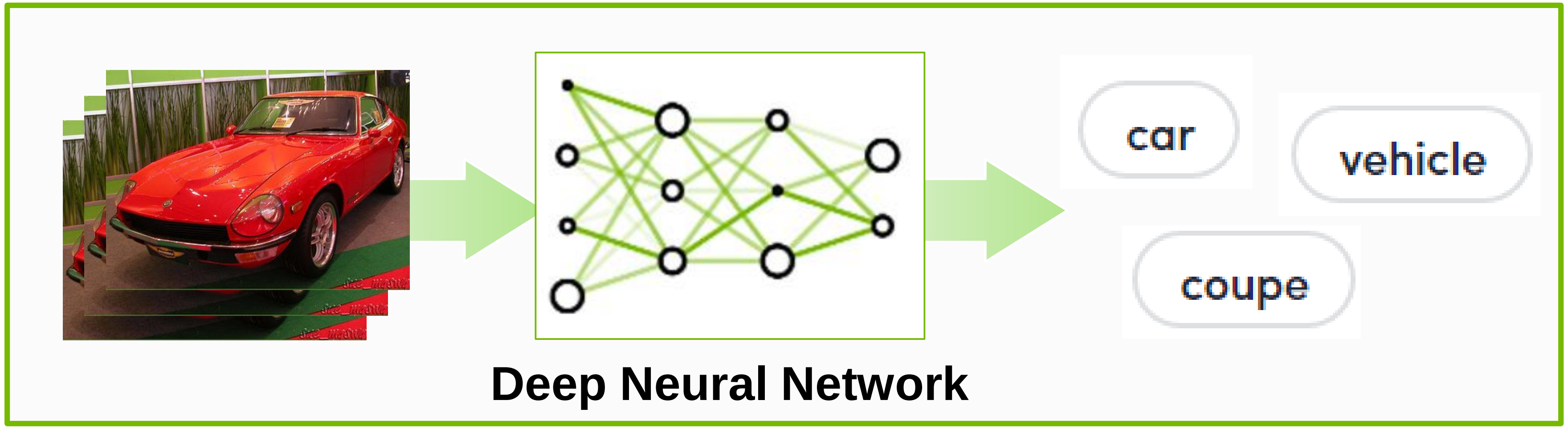


Deep Learning Approach

- ✓ Learn from data
- ✓ Easily to extend
- ✓ Speedup with GPUs

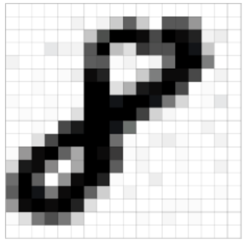
DEEP NEURAL NET

A very simple universal approximator

Universal approximation theorem (Hornik, 1991)

“a single hidden layer neural network with a linear output unit can approximate any continuous function arbitrarily well, given enough hidden units”

x

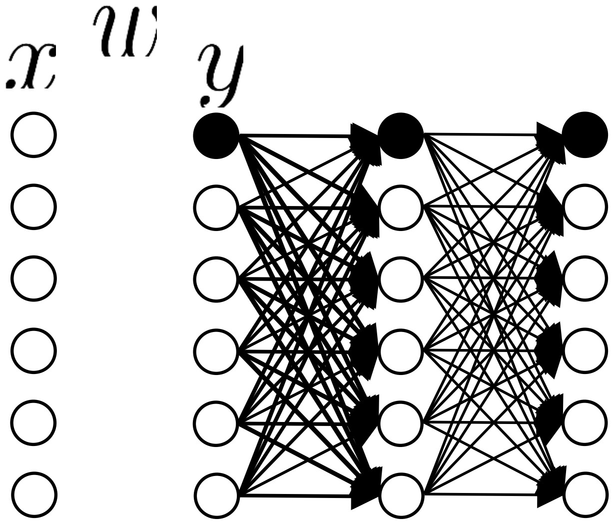


$$y_j = f\left(\sum_i w_{ij} x_i\right)$$

One layer

$$f(x) = \begin{cases} 0, & x < 0 \\ x, & x \geq 0 \end{cases}$$

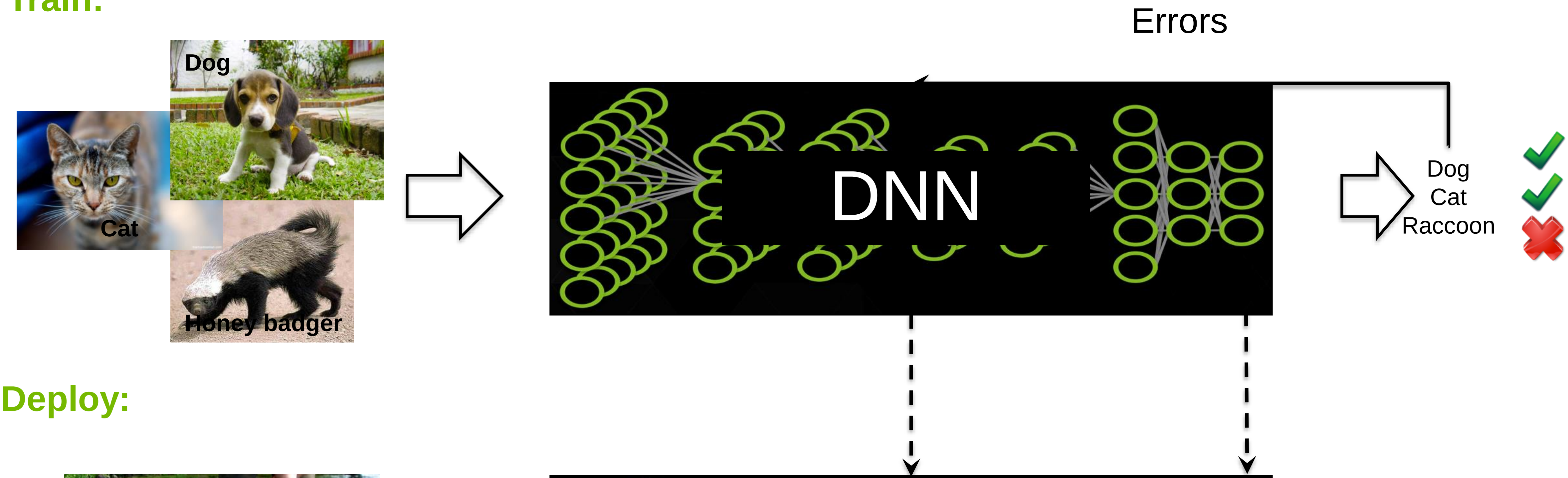
nonlinearity



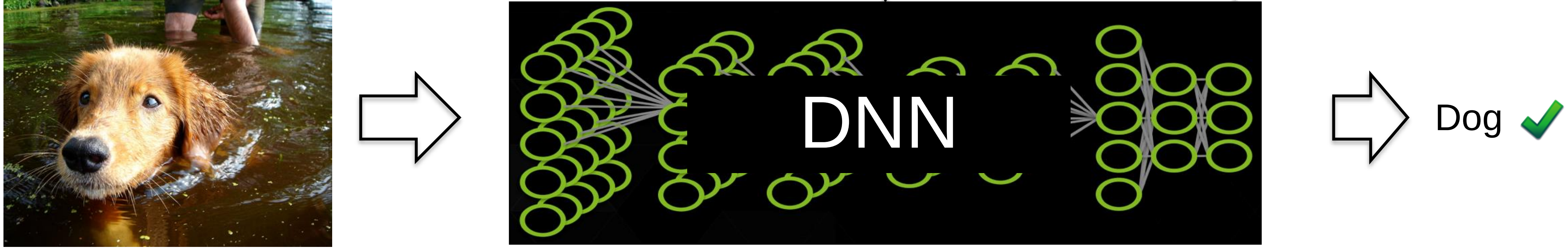
Deep Neural Net

DEEP LEARNING APPROACH

Train:



Deploy:



WHY DEEP LEARNING

Scale Matters

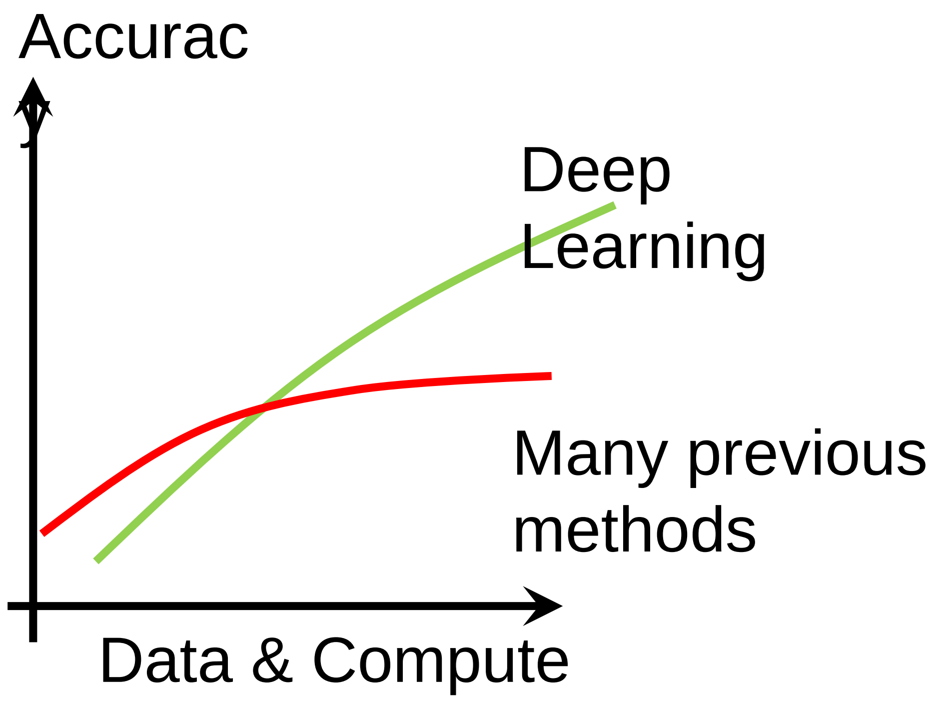
Millions to Billions of parameters

Data Matters

Regularize using more data

Productivity Matters

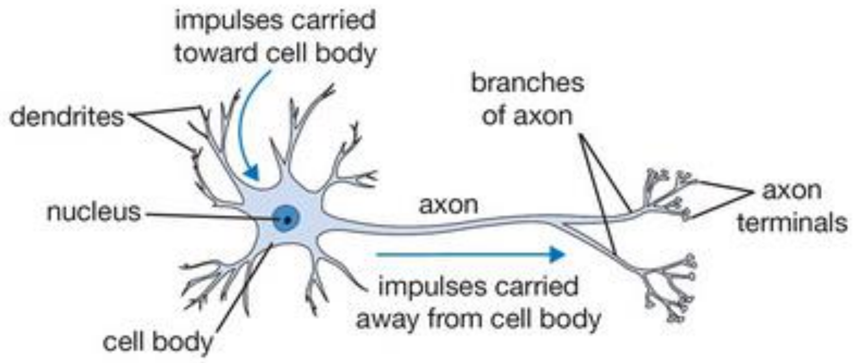
It’s simple, so we can make tools



Deep learning is most useful for large problems

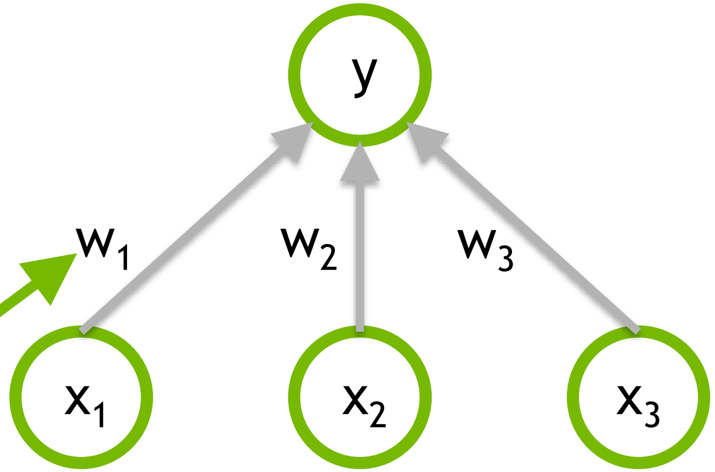
ARTIFICIAL NEURONS

Biological neuron



From Stanford cs231n lecture notes

Artificial neuron

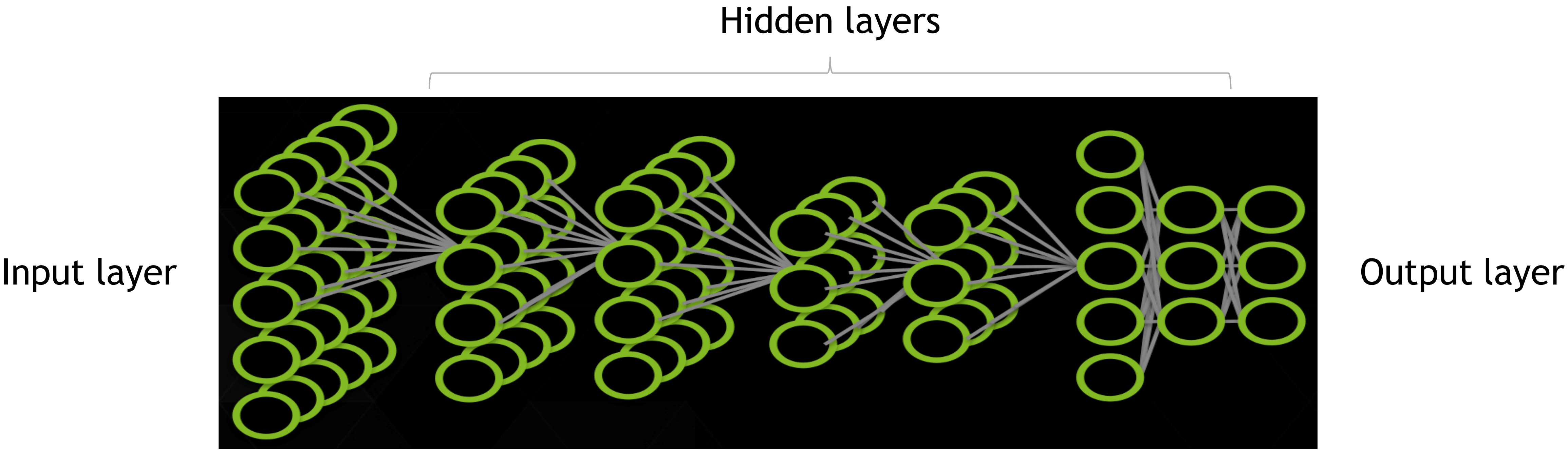


Weights (W_n)
= parameters

$y=F(w_1x_1+w_2x_2+w_3x_3)$

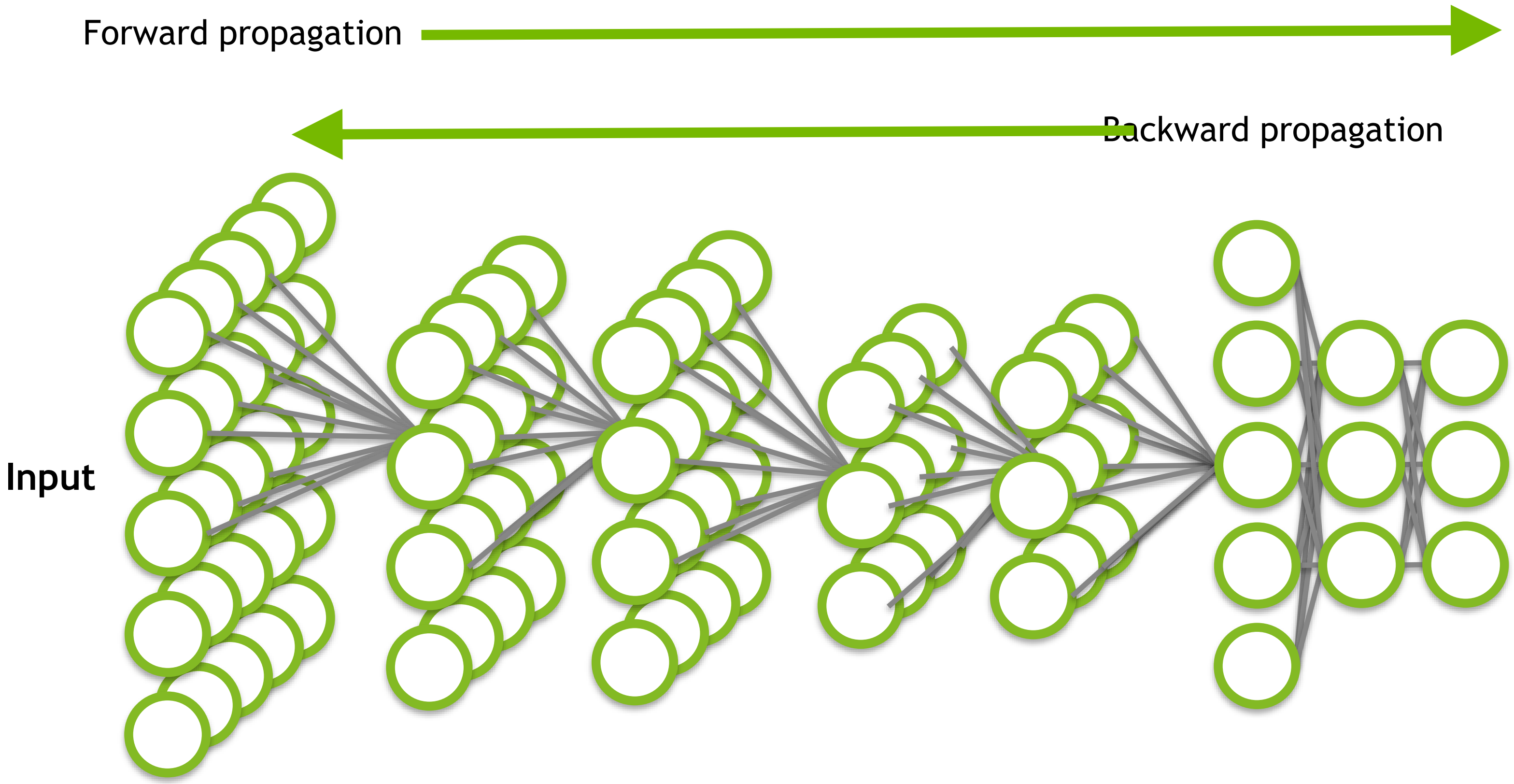
ARTIFICIAL NEURAL NETWORK

A collection of simple, trainable mathematical units that collectively learn complex functions



Given sufficient training data an artificial neural network can approximate very complex functions mapping raw data to output decisions

DEEP LEARNING APPROACH - TRAINING



Process

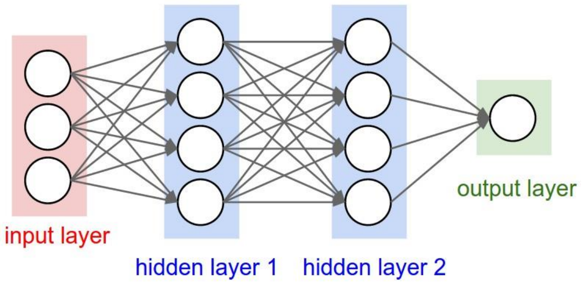
- Forward propagation yields an inferred label for each training image
- Loss function used to calculate difference between known label and predicted label for each image
- Weights are adjusted during backward propagation
- Repeat the process

Deep Learning Categories

Main research areas and breakthroughs of DL

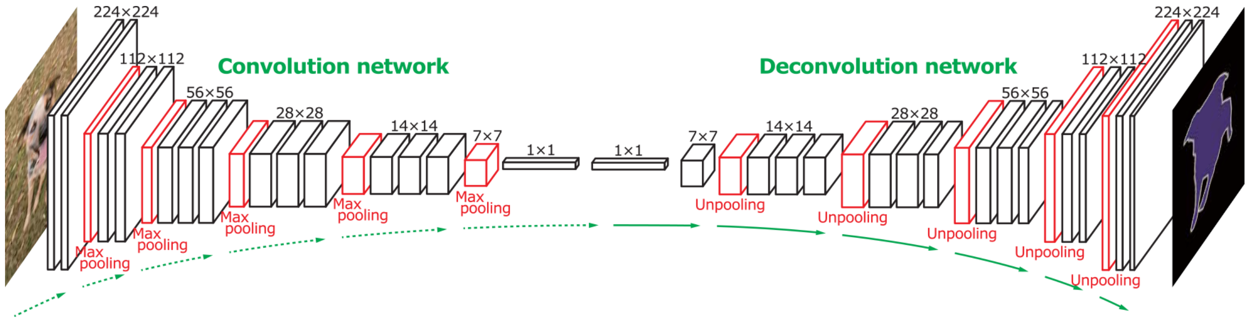
General Deep Learning

Fully-Connected (FC)



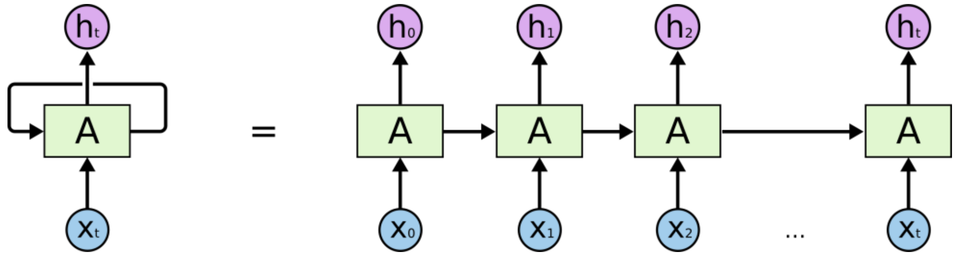
2D/3D Image model

CNN, FCN, etc.

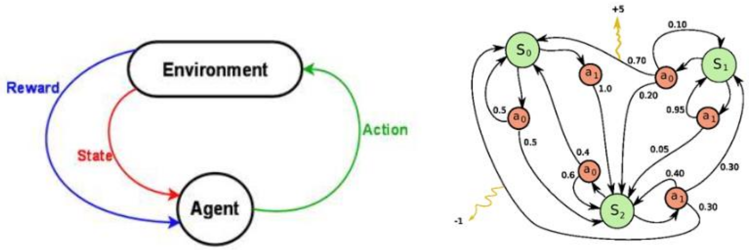


1D Sequence Model

RNN, LSTM, etc.

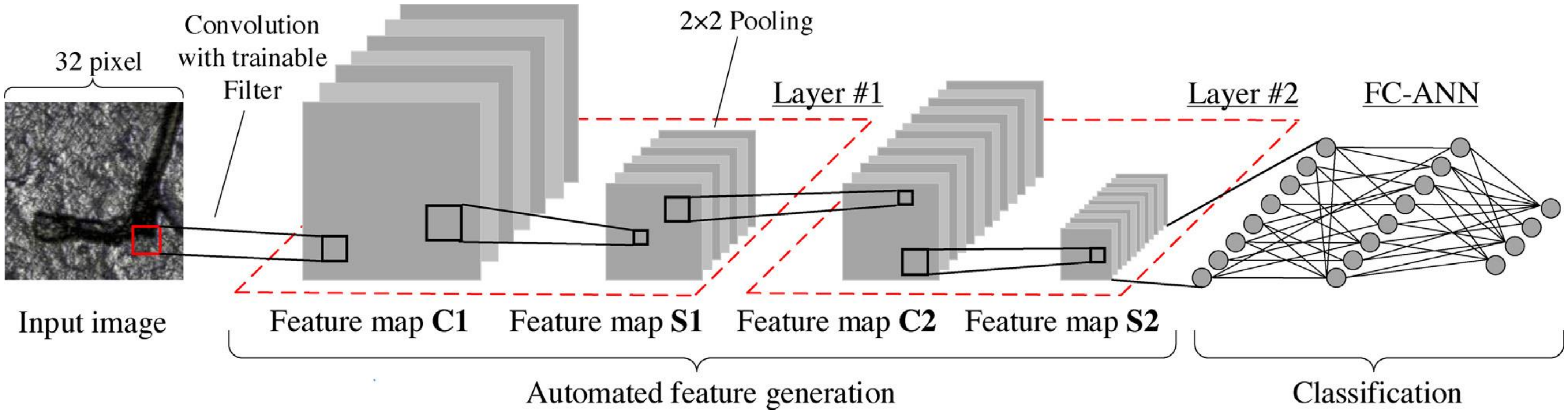


Others: unsupervised DL, reinforce Learning



CNN STRUCTURE

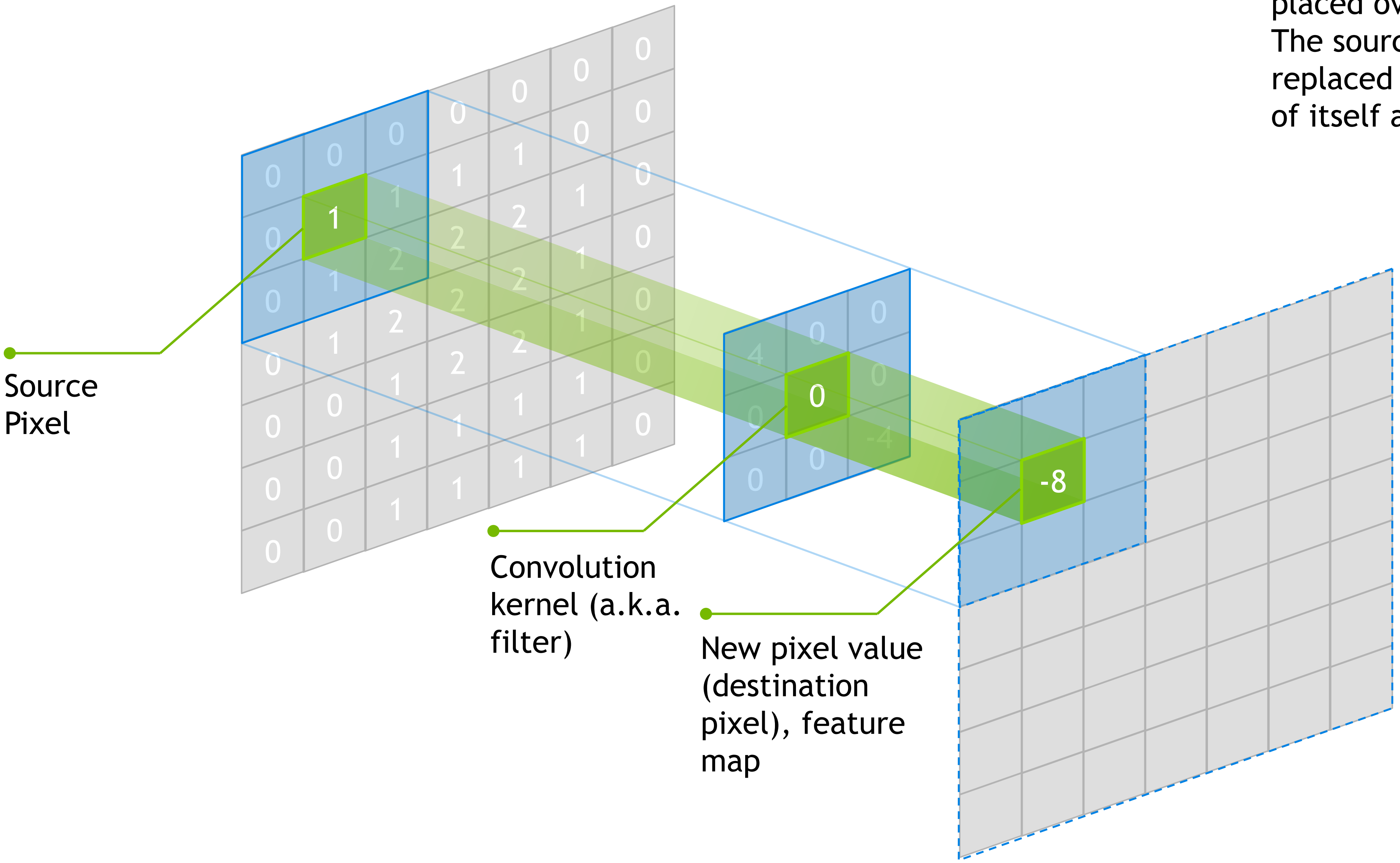
LeNet



Source: Design of Deep Convolutional Neural Network Architectures for Automated Feature Extraction in Industrial Inspection, D. Weimer et al, 2016

CONVOLUTION

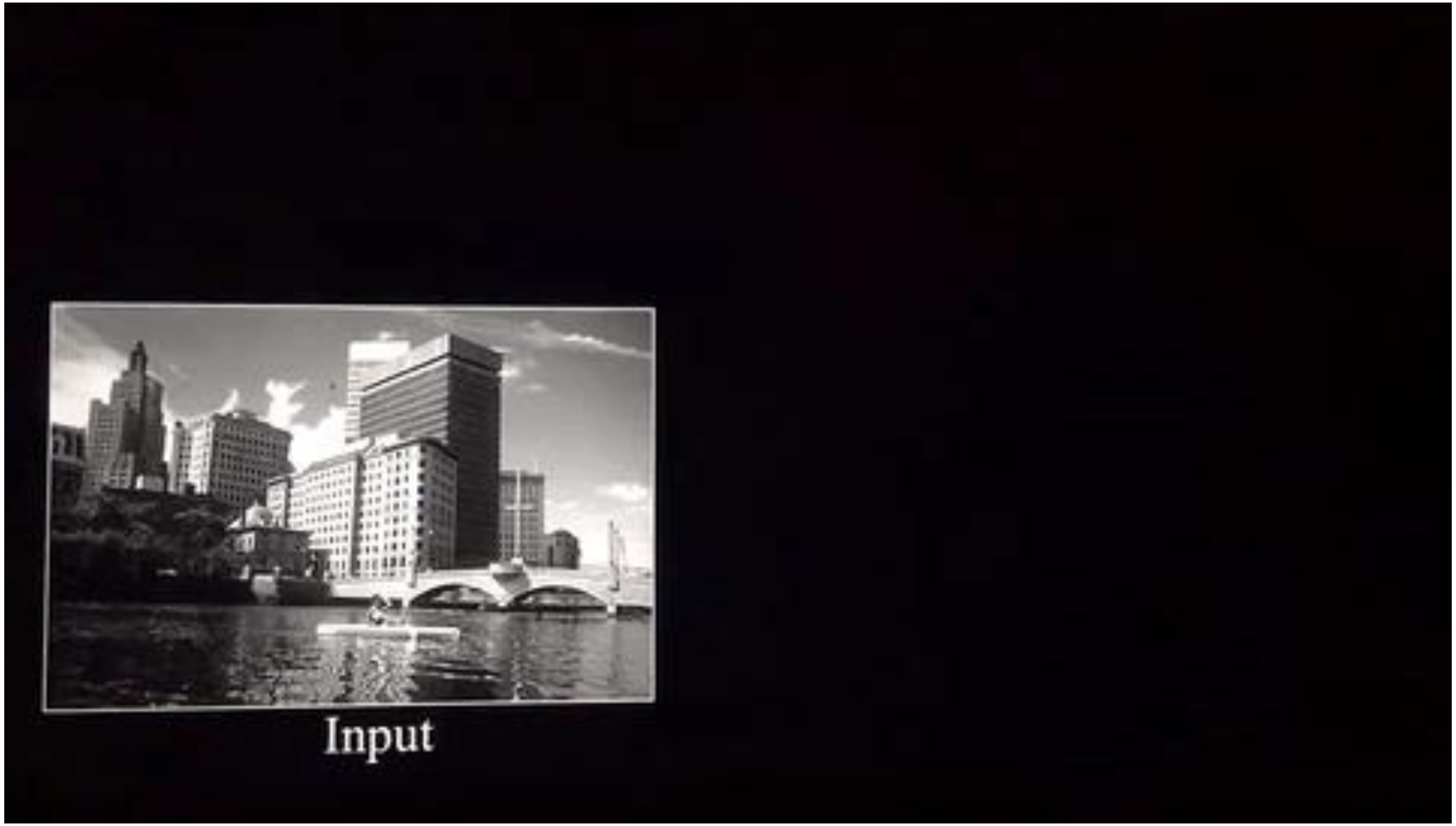
Center element of the kernel is placed over the source pixel. The source pixel is then replaced with a weighted sum of itself and nearby pixels.



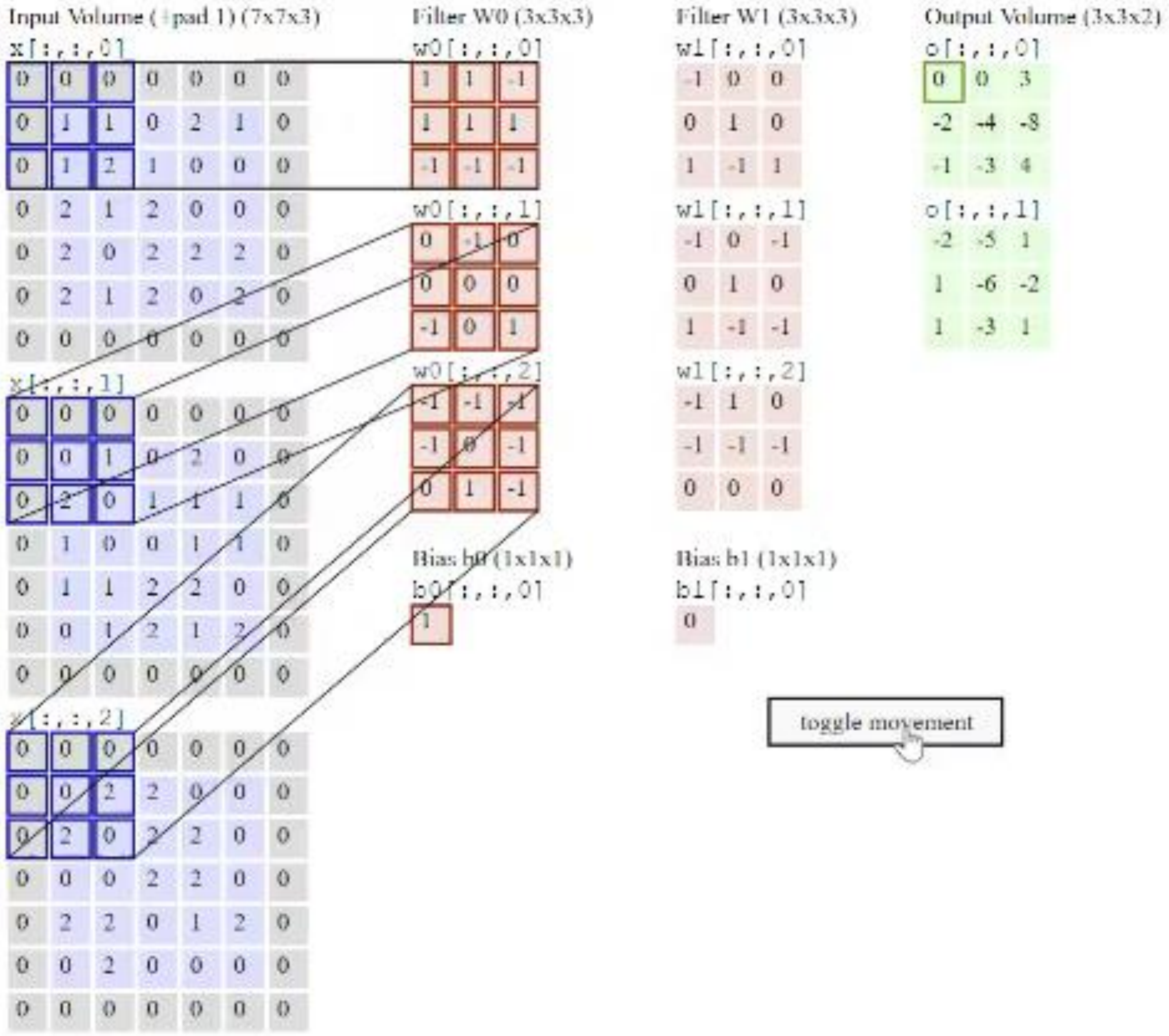
Operation	Filter	Convolved Image
Identity	$\begin{bmatrix} 0 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 0 \end{bmatrix}$	
Edge detection	$\begin{bmatrix} 1 & 0 & -1 \\ 0 & 0 & 0 \\ -1 & 0 & 1 \end{bmatrix}$	
	$\begin{bmatrix} 0 & 1 & 0 \\ 1 & -4 & 1 \\ 0 & 1 & 0 \end{bmatrix}$	
	$\begin{bmatrix} -1 & -1 & -1 \\ -1 & 8 & -1 \\ -1 & -1 & -1 \end{bmatrix}$	
Sharpen	$\begin{bmatrix} 0 & -1 & 0 \\ -1 & 5 & -1 \\ 0 & -1 & 0 \end{bmatrix}$	
Box blur (normalized)	$\frac{1}{9}\begin{bmatrix} 1 & 1 & 1 \\ 1 & 1 & 1 \\ 1 & 1 & 1 \end{bmatrix}$	
Gaussian blur (approximation)	$\frac{1}{16}\begin{bmatrix} 1 & 2 & 1 \\ 2 & 4 & 2 \\ 1 & 2 & 1 \end{bmatrix}$	

CONVOLUTION

How convolve works?

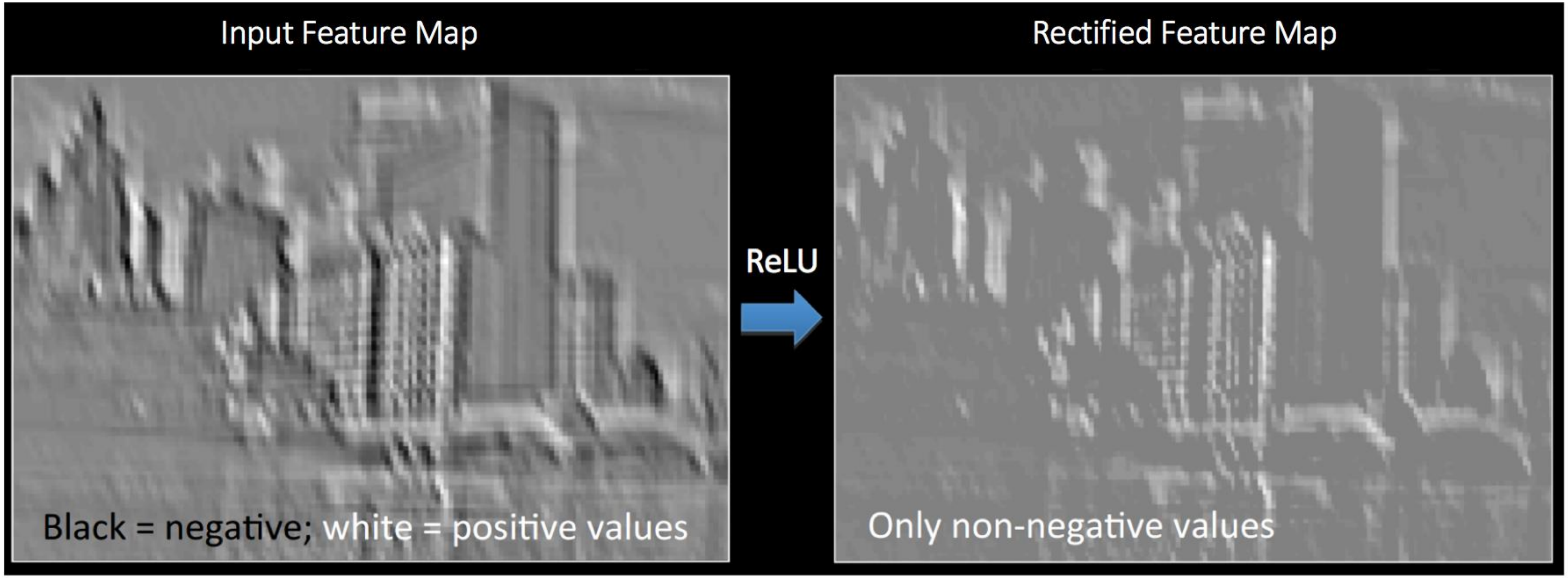


CONVOLUTION with depth



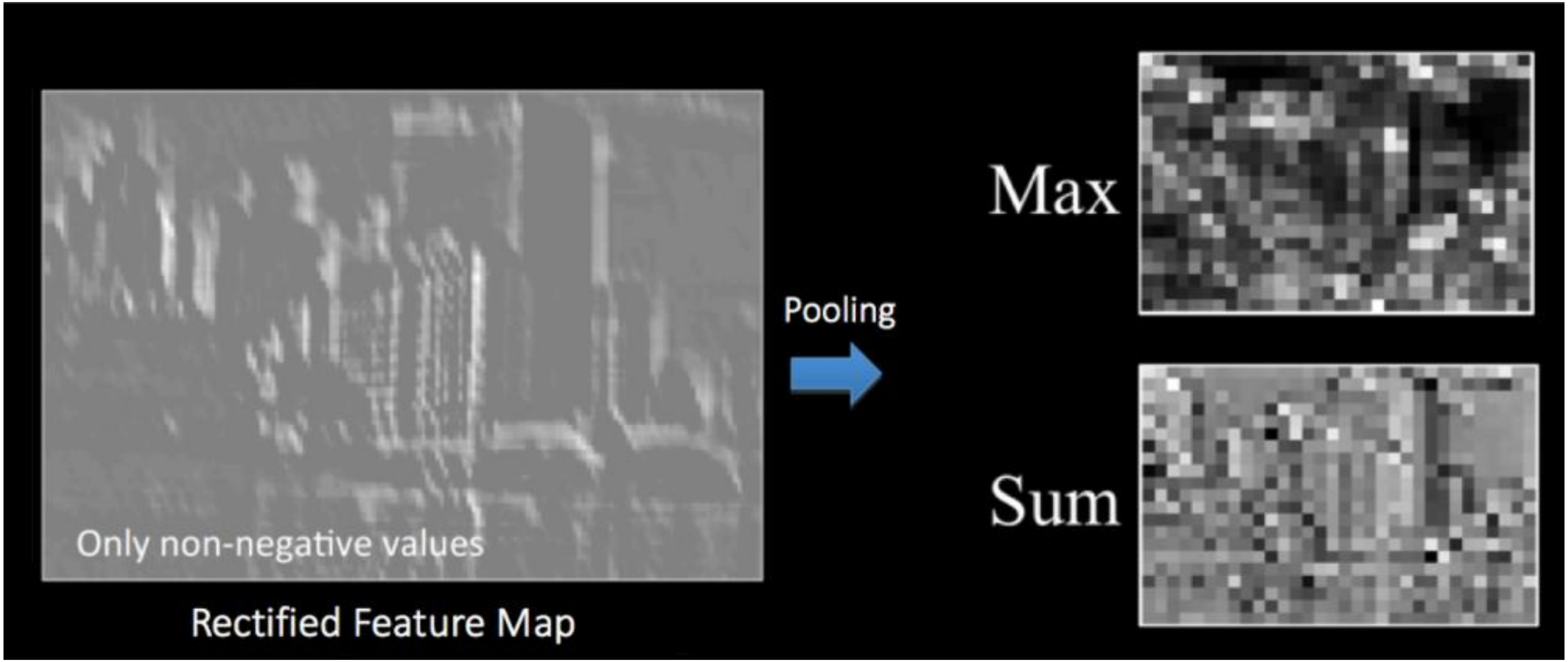
ACTIVATE FUNCTION

Relu, Sigmoid, tahn

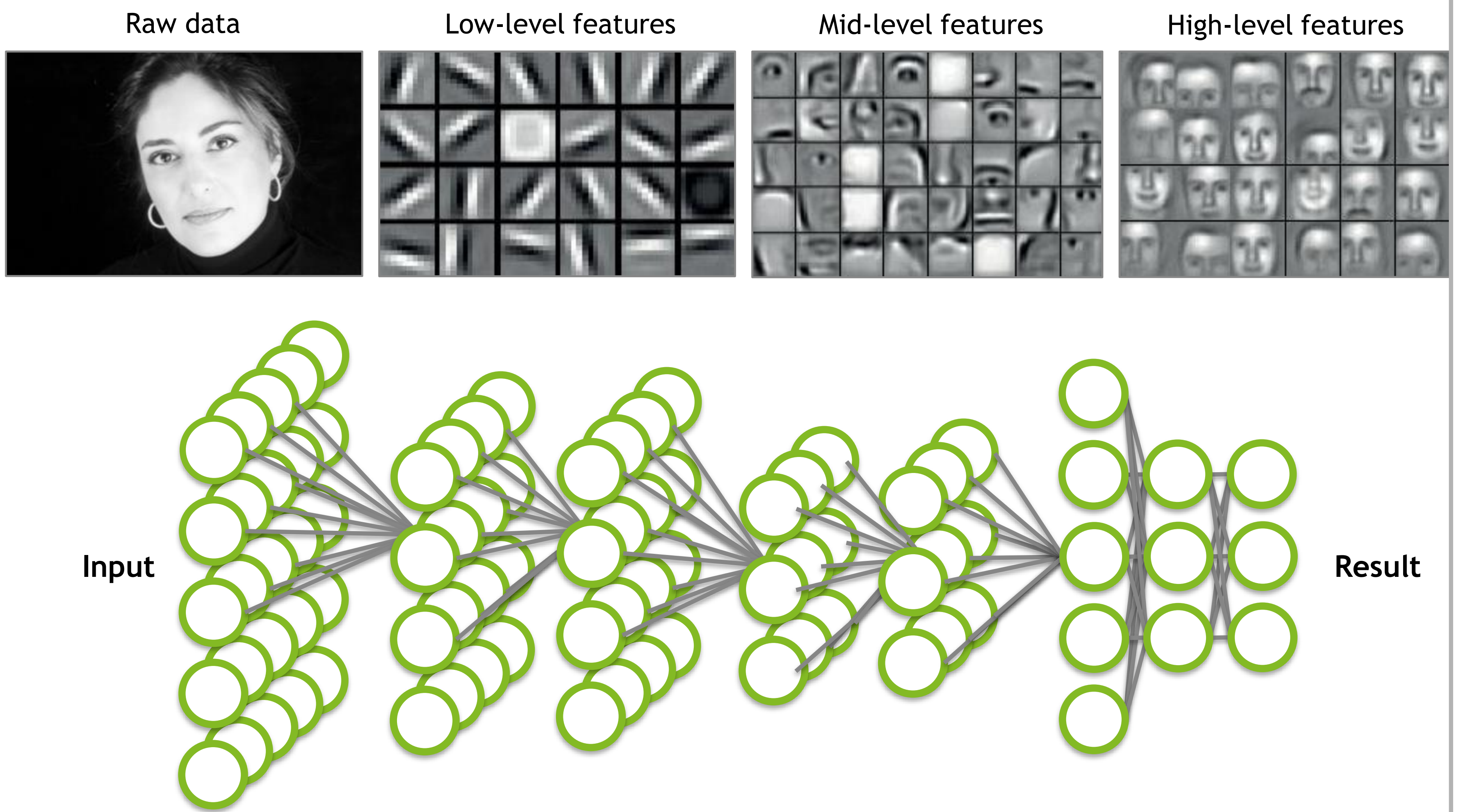


POOLING

max pooling, average pooling



DEEP NEURAL NETWORK (DNN)



Application components:

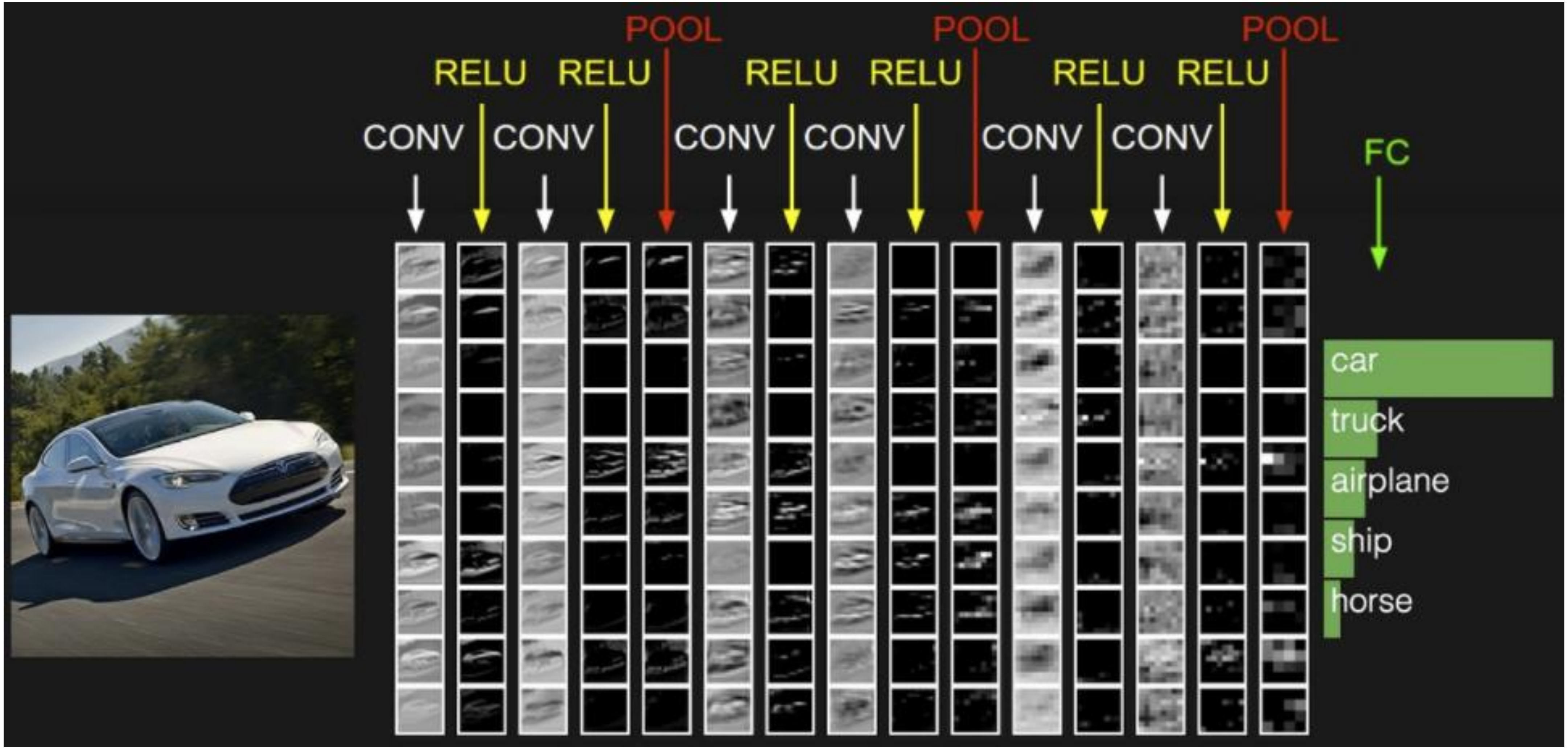
Task objective
e.g. Identify face

Training data
10-100M images

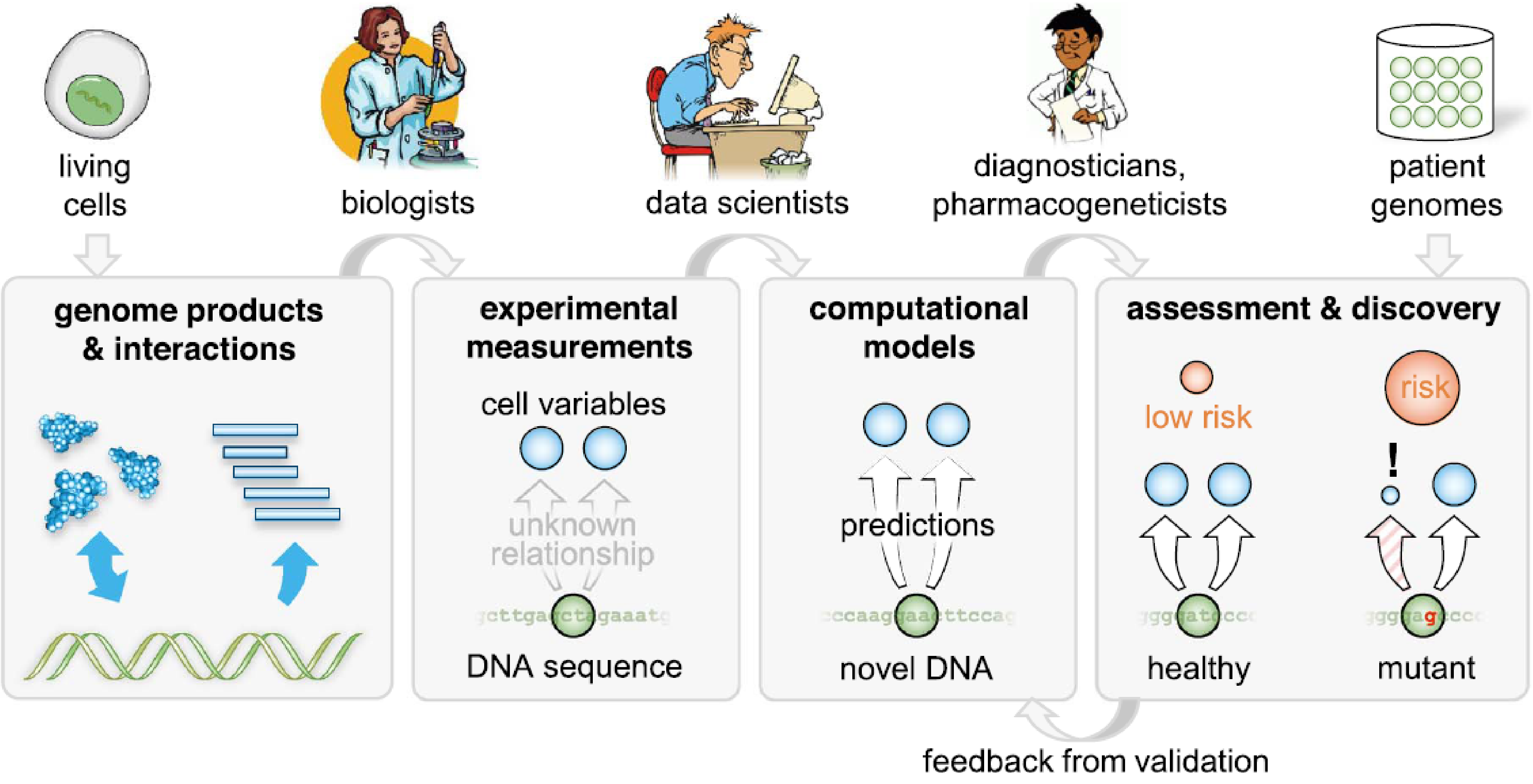
Network architecture
~10s-100s of layers
1B parameters

Learning algorithm
~30 Exaflops
1-30 GPU days

VGG ACTIVATIONS OF EACH VOLUMN



SIMPLE WORKFLOW



DECODING HUMAN GENOME

TGCCAAGCAGCAAAGTTTTGCTGCTGTTTATTTTTGTAGCTCTTACTATATT
CTACTTTTACCATTGAAAATATTGAGGAAGTTATTTATATTTCTATTTTTTAT
ATATTATATATTTTATGTATTTTAATATTACTATTACACATAATTATTTTTTAT
ATATATGAAGTACCAATGACTTCCTTTTCCAGAGCAATAATGAAATTTCAC
AGTATGAAAATGGAAGAAATCAATAAAATTATACGTGACCTGTGGCGAAG
TACCTATCGTGGACAAGGTGAGTACCATGGTGTATCACAAATGCTCTTTCC
AAAGCCCTCTCCGCAGCTCTTCCCCTTATGACCTCTCATCATGCCAGCATTA
CCTCCCTGGACCCCTTTCTAAGCATGTCTTTGAGATTTTCTAAGAATTCTTA
TCTTGGCAACATCTTGTAGCAAGAAAATGTAAAGTTTTCTGTTCCAGAGCC
TAACAGGACTTACATATTTGACTGCAGTAGGCATTATATTTAGCTGATGAC
ATAATAGGTTCTGTCATAGTGTAGATAGGGATAAGCCAAAATGCAATAAG
AAAAACCATCCAGAGGAAACTCTTTTTTTTTTCTTTTTCTTTTTTTTTTTTCCA
GATGGAGTCTCGCACTTCTCTGTCACCCGGGCTGGAGCGCAGTGGTGCAA
TCTTGGCTCACTGCAACCTCCACCTCCTGGGTTCAGGTGATTCTCCCACCTC
AGCCTCCCGAGTAGTAGCTGGAATTACAGGTGCGCGCTCCCACACCTGGC
TAATTTTTTGTATTCTTAGTAGAGATGGGGTTTCACCATGTTGGCCAGGCT
GGTCTCAAACTCCTGCCCTCAGGTGATCTGCCCACCTTGGCCTCCCAGTGT
TGGGTTTACAGGCGTGAGCCACCGCGCCTGGCCTGGAGGAAACTCTTTAT
AACTACCGAGTGGTGATGCTGAAGGGAGACACAGCCTTGGATATGCGAG
GACGATGCAGTGCTGGACAAAAGGCAGGTATCTCAAAAGCCTGGGGAGC
CAACTCACCCAAGTAACTGAAAGAGAGAAACAAACATCAGTGCAGTGGA
AGCACCCAAGGCTACACCTGAATGGTGGGAAGCTCTTTGCTGCTATATAA
AATGAATCAGGCTCAGCTACTATTATT ....

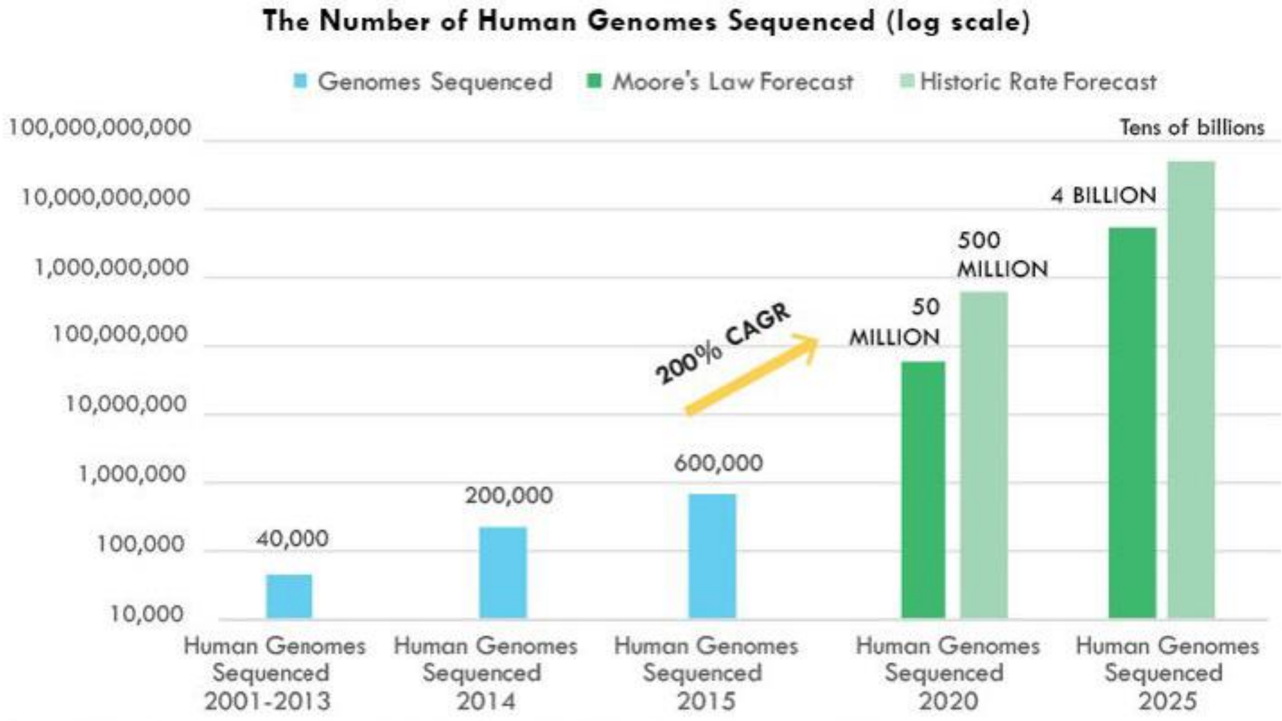
Function?

The Human Genome Project

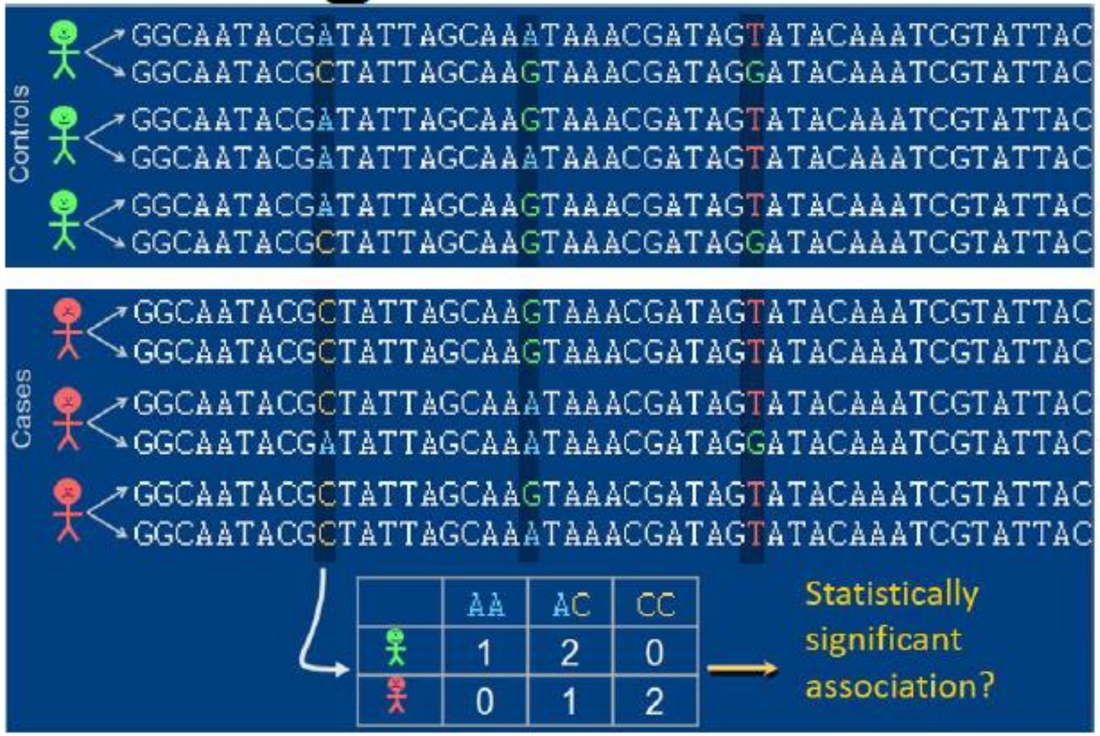
2003

~ 3 billion nucleotides

Population sequencing identifies genetic variants

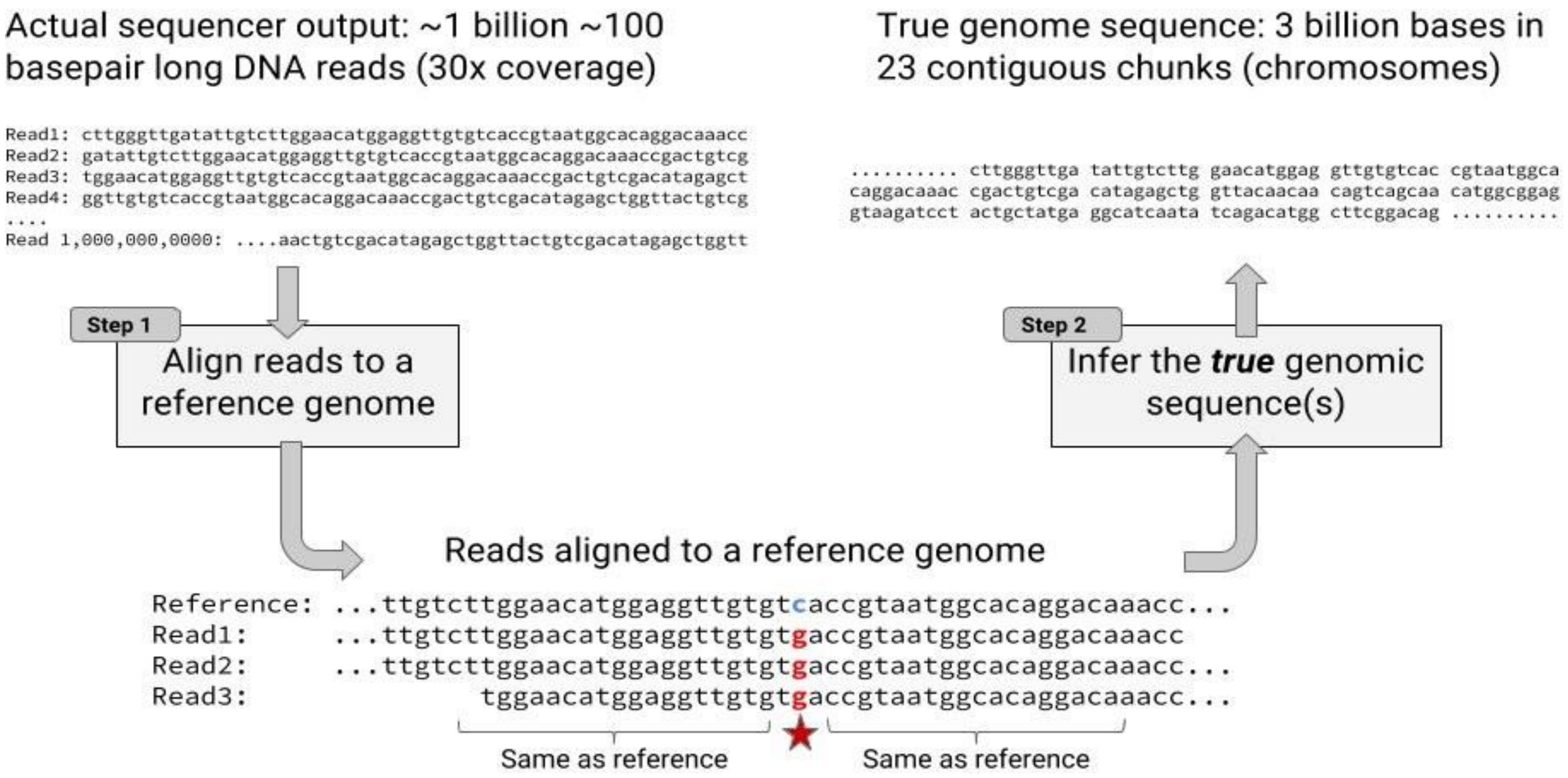


Source: National Human Genome Research Institute (NHGRI), ARK Investment Management LLC



- 100,000s of personal genomes (**<u>population-scale sequencing</u>**)
- Millions of **<u>genetic variants</u>** (mutations) across individuals
- **<u>Which variants are</u>** benign and which ones are **<u>related to disease</u>**?
- What **<u>functional DNA words</u>** are these disease-associated variants disrupting?

VARIANT



Actual sequencer output: ~1 billion ~100 basepair long DNA reads (30x coverage)
Read1: cttgggttgatattgtcttggaacatggaggttgtgtcaccgtaatggcacaggacaaacc
Read2: gatattgtcttggaacatggaggttgtgtcaccgtaatggcacaggacaaaccgactgtcg
Read3: tggaacatggaggttgtgtcaccgtaatggcacaggacaaaccgactgtcgacatagagct
Read4: ggttgtgtcaccgtaatggcacaggacaaaccgactgtcgacatagagctggttactgtcg
....
Read 1,000,000,0000: ....aactgtcgacatagagctggttactgtcgacatagagctggtt
True genome sequence: 3 billion bases in 23 contiguous chunks (chromosomes)
.... cttgggttga tattgtcttg gaacatggag gttgtgtcac cgtaatggca
caggacaaac cgactgtcga catagagctg gttacaacaa cagtcagcaa catggcggag
gtaagatcct actgctatga ggcatcaata tcagacatgg cttcggacag ....
Step 1
Align reads to a reference genome
Step 2
Infer the *true* genomic sequence(s)
Reads aligned to a reference genome
Reference: ...ttgtcttggaacatggaggttgtgtcaccgtaatggcacaggacaaacc...
Read1: ...ttgtcttggaacatggaggttgtgtgaccgtaatggcacaggacaaacc
Read2: ...ttgtcttggaacatggaggttgtgtgaccgtaatggcacaggacaaacc...
Read3: tggaacatggaggttgtgtgaccgtaatggcacaggacaaacc...
Same as reference
Same as reference

Recasting variant calling for deep learning

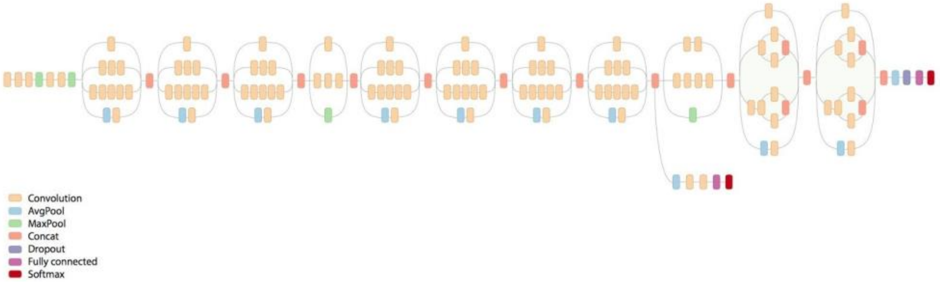
Encode reads and reference as images

True SNPs

True Indels

False variants

Use inception-v3 to call variant genotype



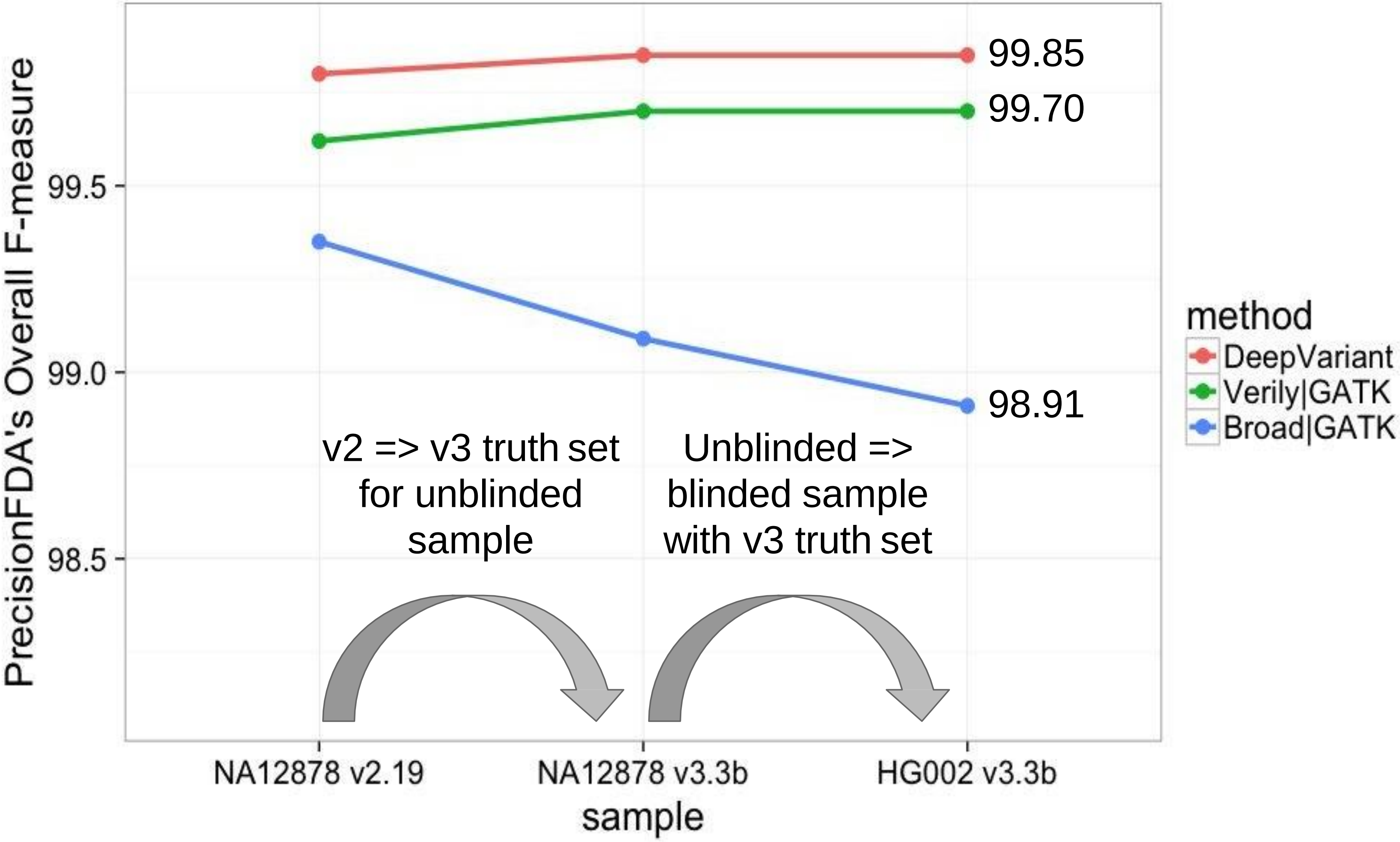
Train on Genome in a Bottle sample using their genotype labels

Each germline WGS dataset provides e.g., ~3.7M labeled varaints for training:

- 215K false positives candidates
- 2.1M true heterozygotes
- 1.3M true homozygous alternates

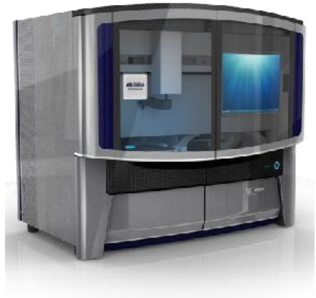
Encoding is roughly red = {A,C,G,T}; green = {quality score}; blue = {read strand}; alpha = {matches ref genome}

DeepVariant won an award at the 2016 PrecisionFDA competition



F-measure is the harmonic mean of precision and recall.

DeepVariant can learn to call variants in many sequencing technologies

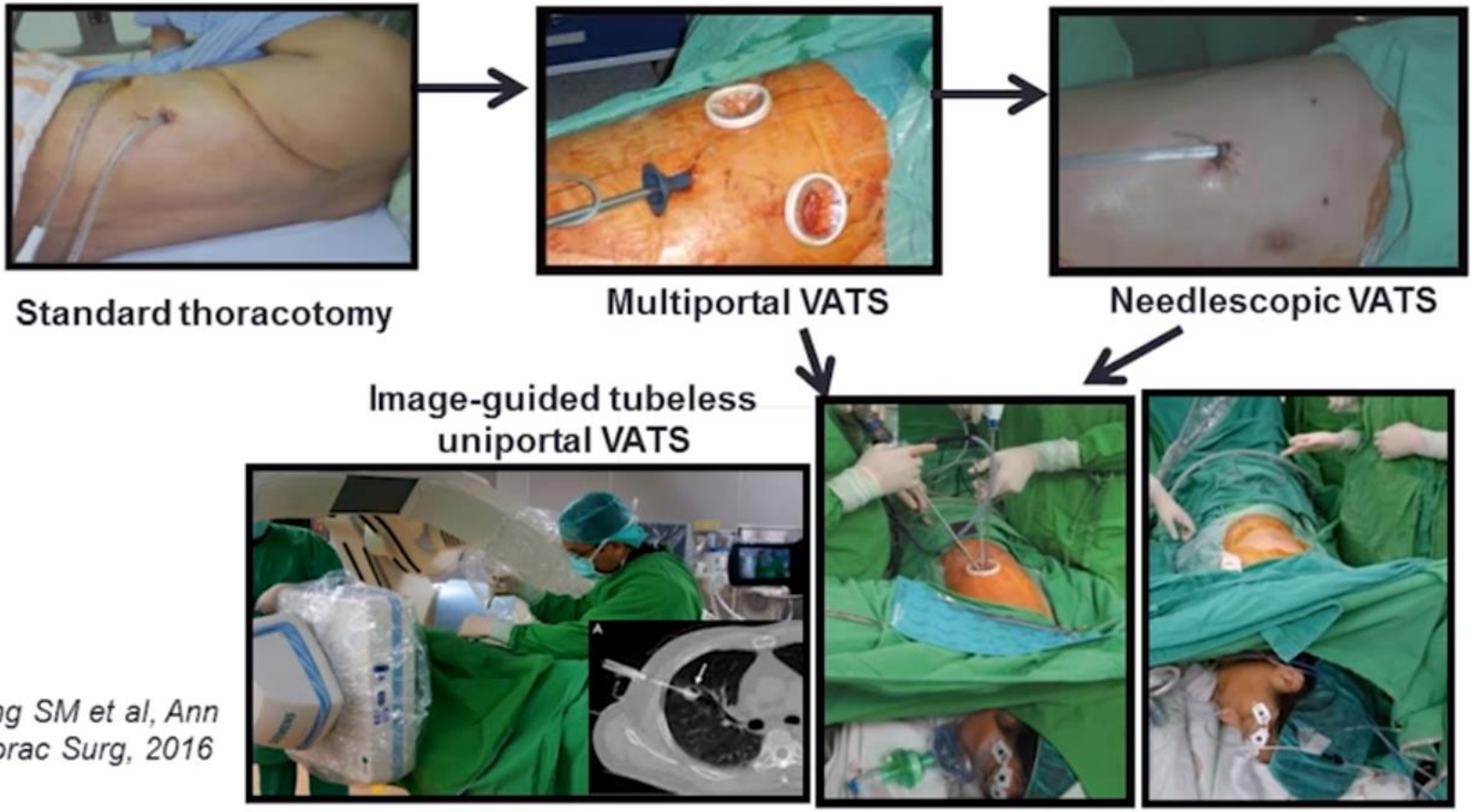


Dataset	10X Chromium 75x WGS	PacBio raw reads 40x WGS	SOLID SE 85x WGS	Illumina TruSeq exome
DeepVariant (F1 metric)	**99.3%**	**92.7%**	**86.4%**	**96.1%**
Comparator (F1 metric)	98.2%	56.1%[1]	78.8%[2]	95.4%
Comparator caller	Long Ranger	samtools	GATK	ensemble

[1]No standard caller exists for this technology for human samples;
[2]Old technology without any maintained variant callers.

LUNG CANCER SURGERY

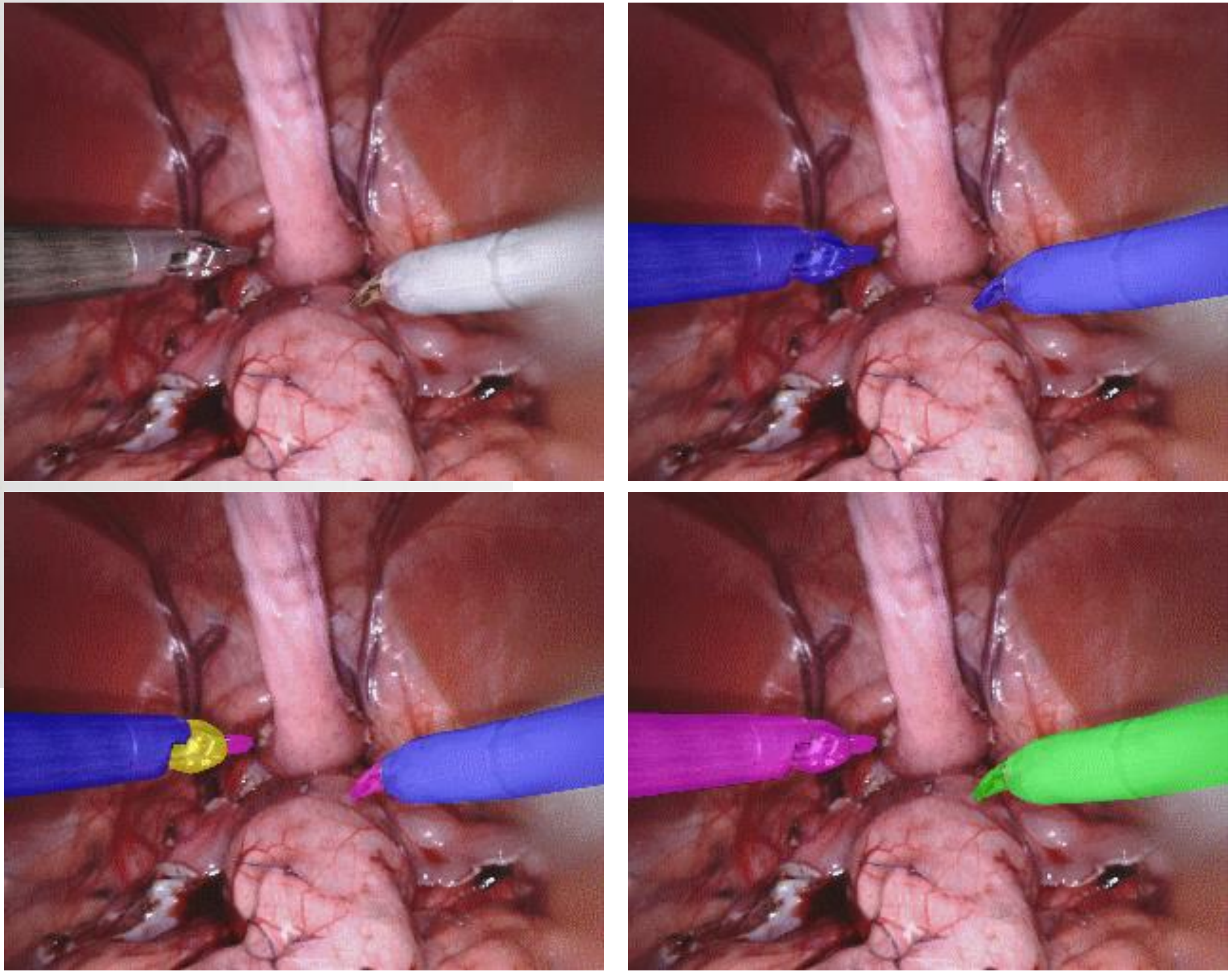
Tubeless Uniportal VATS



Yang SM et al, Ann Thorac Surg, 2016

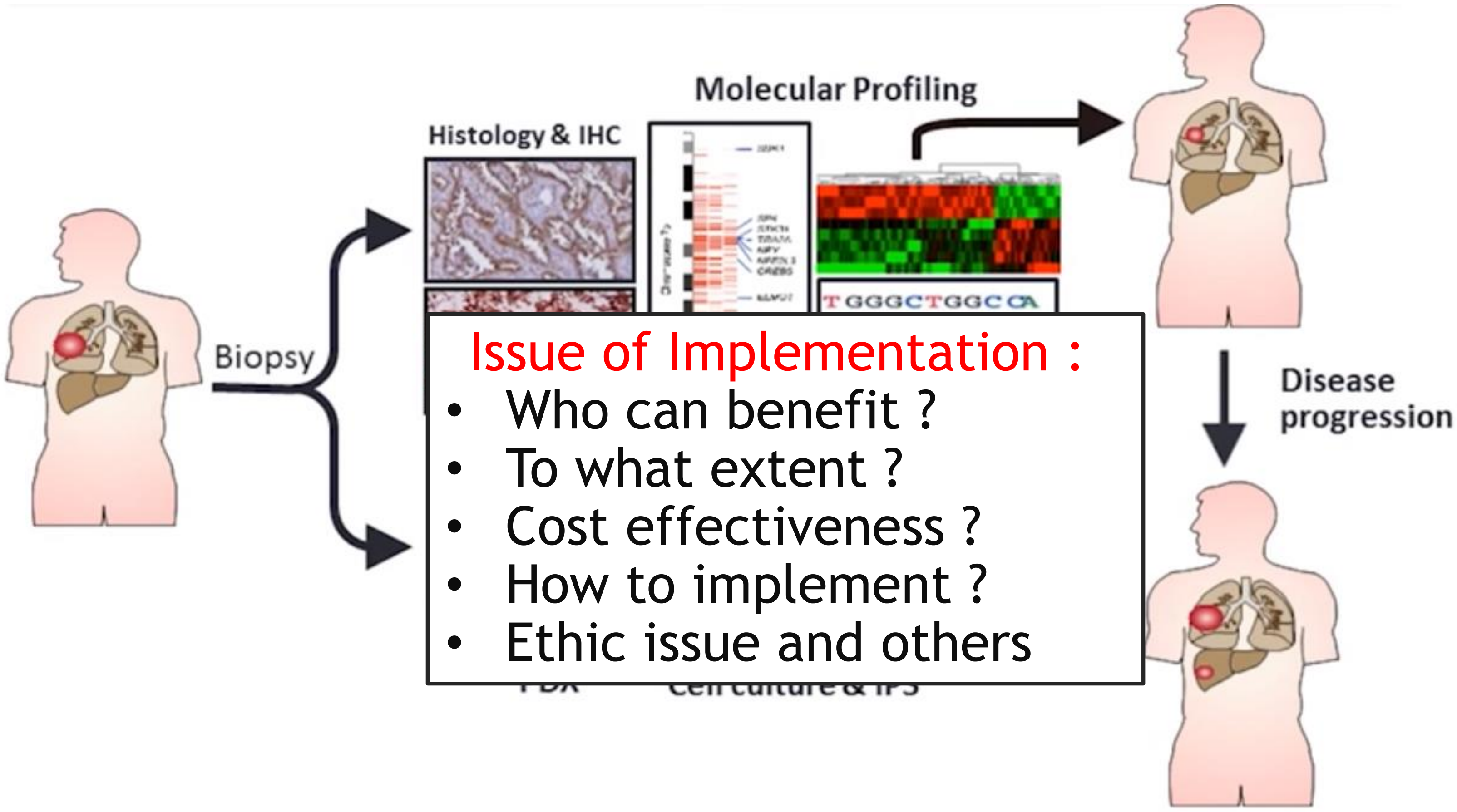
DA VINCI MACHINE SURGERY

Deep Learning in Da Vinci machine



- Correctly detect an instrument's position.
- Accurate pixel-wise segmentation in the vicinity of surgical scenes.

CURRENT PRACTICE FOR PRECISION CANCER THERAPY



Issue of Implementation :

- Who can benefit ?
- To what extent ?
- Cost effectiveness ?
- How to implement ?
- Ethic issue and others

GENOMIC PROFILING SHOULD BE CONSIDERED A TOOL FOR IMPROVING OUTCOMES FROM THE START

- Research advances
- Clinical trail designs
- FDA Policy
- Pharma conscience
- Philanthropy support
- Patient compliance

- improving the accuracy of diagnosis
- helping determine prognosis
- predicting response to certain therapies
- enabling avoidance of chemotherapy and its associated side effects