

## EE 428/528 BioMEMS & Lab-on-a-chip

### Lecture 07: Miniaturization in the Life Sciences 1



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## [Life Science] Life and Medical Sciences for Engineers

### Biotechnology

- ◆ Primarily focused on the chemistry and low-level understanding of living systems. Cell biology, molecular biology, biochemistry, etc.
- ◆ Primary market is pharmaceuticals (drugs). Also markets in point-of-care diagnostics, food industry, and agriculture.

### Biomedical

- ◆ Primarily focused on the human physiological system and how to repair it. Physiology, surgery, etc.
- ◆ Primary market is the medical industry (including implants, imaging, prosthetics, minimally invasive systems). Also markets in human systems, bionics, and environmental sensing.

### Key needs

- ◆ Miniaturization needs in biotech are generally associated with the need to reduce the cost of "Drug Discovery".
- ◆ Miniaturization leads to smaller volumes, higher throughput, faster experiments, automation, all of which lead to improved drug discovery at lower cost.
- ◆ Technology development tends to be in areas of microfluidics, nanovolume chemistry, and highly parallel systems.

## [Life Science] Drugs 101

### Cellular and molecular biology: Nature's nanotechnology

- ◆ Today we understand life sciences at the molecular level—wondrous complex systems composed of millions of nanomachines, nanostructures and nanomaterials working in harmony.

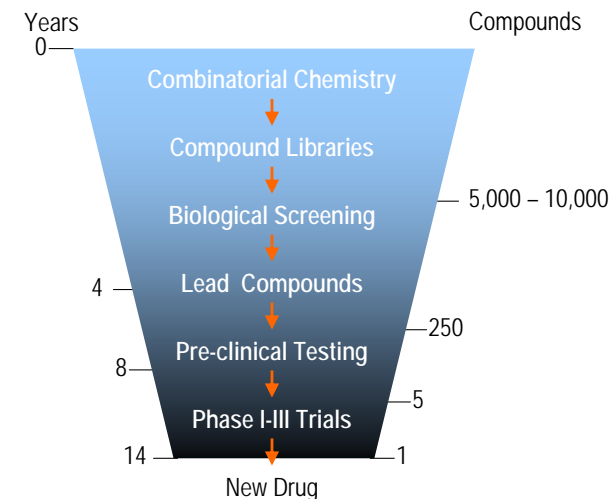
### Drugs: molecular medicine

- ◆ Modern drugs work by specific molecular interaction with biological molecules in the cells.
- ◆ Drugs have become the "wonder cure" for many ailments, and have dramatically improved the quality of human life.

## [Life Science] Drug Development

### Drug Development Process

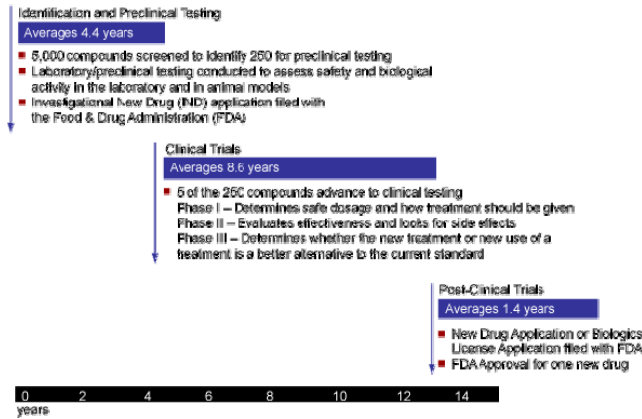
- ◆ Unfortunately, finding the drugs that will cure today's and tomorrow's diseases is difficult, time consuming and very, very expensive.
- ◆ \$100-800 M
- ◆ 10-15 Years



## [Life Science] Drug Development Timeline

### From drug discovery to approved drug

- Process starts with "hits"—candidate molecules that might be successful drugs. The next 10 to 15 years are spent eliminating bad candidates to find one successful drug. Cost increases with time. Highest costs are in clinical trials and FDA approval.



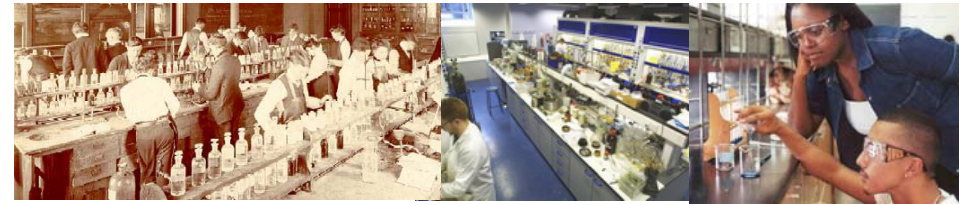
## [Life Science] Drug Development Paradigm (before 1990s)

### Hypothesis Driven Drug Development

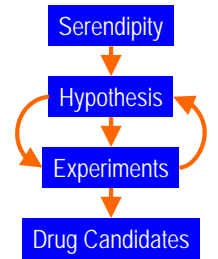
- Drug development has always been difficult, and to a great extent, dependent upon serendipity. Drug discovery has required brilliant minds to toil to isolate and identify cures for disease.
- Penicillin discovered in 1928 by chance.

### Drug Research

- Our understanding of life sciences has dramatically improved in recent years, but the way we do most research is not so different from earlier generations.



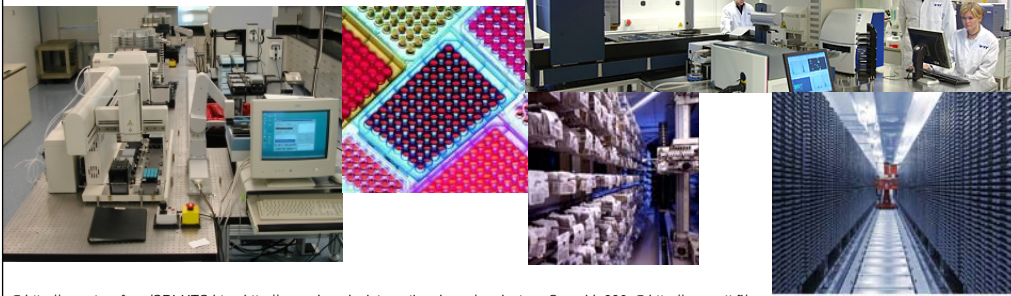
### Hypothesis Driven Drug Development



## [Life Science] Paradigm Shift (since 1990s)

### High Throughput Technology

- Computerized automated instruments, bioinformatics, and miniaturized systems are revolutionizing the way life science is done.
- Machines can increase throughput by thousands. This is the technology of "high throughput" systems.



## [Life Science] Drug Discovery Paradigm

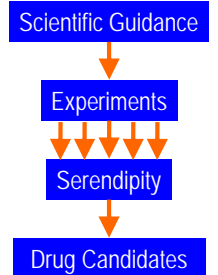
### Drug Discovery

- Miniaturization, Automation and Computation. These engineering advancements have enabled a revolution in life science research.
- New paradigm is **Drug Discovery**

### Human Genome Project

- Begun formally in 1990, the U.S. Human Genome Project was a 13-year effort coordinated by the U.S. Department of Energy and the National Institutes of Health.
- The project originally was planned to last 15 years, but rapid technological advances accelerated the completion date to 2003.
  - Due to high throughput technology by robots
- Sequence and analysis of the human genome working draft was published in February 2001 and April 2003 issues of *Nature and Science*

### Discovery Driven Research



## [Life Science] Need for Massive Automation and Parallelization

### Human Genome Project

**How to Sequence a Genome\***

PLAY ALL... 9min 46s

- Mapping ... 1min 16s
- Building Libraries ... 28s
- Subclones... 35s
- E. coli to store and copy DNA ... 54s
- Preparing DNA for Sequencing ... 16s
- Sequencing Reaction ... 1min 44s
- Products of Sequencing Reaction ... 40s
- Separating the Sequencing Reaction ... 30s
- Reading the Sequencing Reaction ... 28s
- Assembling the Results ... 55s
- Working draft sequence / Conclusion ... 2min

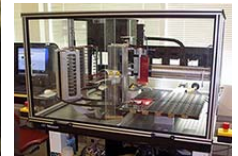
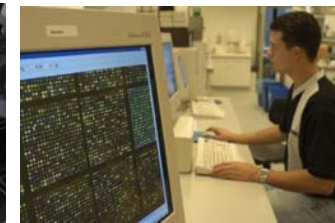
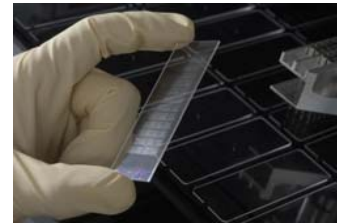
\* This is the approach used by the Human Genome Project to sequence the human genome. For a slightly different strategy, [CLICK HERE](#).

http://www.genome.gov/Pages/EducationKIT/download.html

## [Life Science] Next Paradigm: Intelligent Discovery Paradigm

### Integrated Micro/Nano Systems + Information Technology

- More functionality on micro arrays. Greater sensing capabilities. Greater control. Greater intelligence.
- Microarrays, Microfluidics, NanoBioSensors



Intelligent discovery  
driven research

Scientific Guidance

Experiments

Serendipity

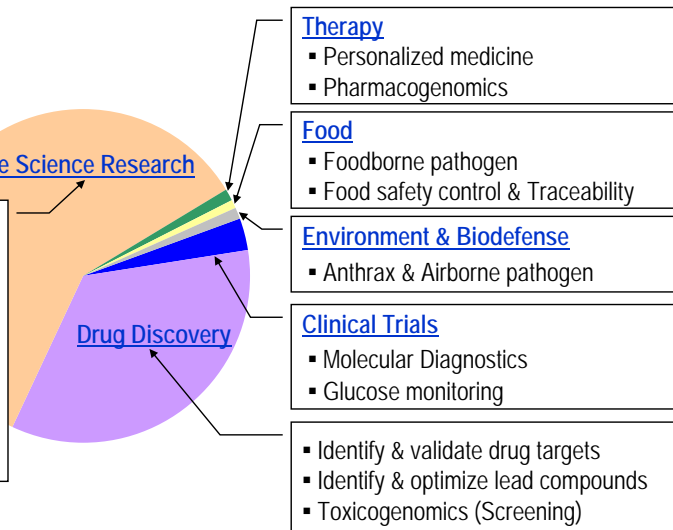
Drug Candidates

http://www.kwfkankerbestrijding.nl/content/pages/DNA\_chip\_vist\_naar\_kankergenomen.html, http://microarray.okstate.edu/arrayers.shtml

## BioChip Applications

### Life Science Research

- Genomics**
  - SNP Genotyping
  - DNA Sequencing analysis
  - Gene expression
- Proteomics**
  - Protein Profiling
  - Protein interaction
- Research Tools**



## BioChip Applications

Type	Applications	Type	Contents	Product Name
Microfluidic - based	Research	Chip	DNA	<ul style="list-style-type: none"> <li>2100 Bioanalyzer &amp; 5100 ALP system (Agilent)</li> <li>Open array system (bioTrove)</li> </ul>
			Protein	<ul style="list-style-type: none"> <li>Topaz system (Fluidigm)</li> <li>CD Microarray (Gyros)</li> </ul>
	Clinical	Chip	Other	<ul style="list-style-type: none"> <li>Lilliput chip (BI microparts)</li> </ul>
			Instrument	<ul style="list-style-type: none"> <li>DNA: GeneXpert system (Cepheid)</li> <li>Other: Piccolo system (Abaxis)</li> </ul>
		Other	<ul style="list-style-type: none"> <li>i-stat (Abbott)</li> </ul>	
	Drug Development	Chip	Other	<ul style="list-style-type: none"> <li>LabChip 3000 Drug Discovery system (Caliper LS)</li> </ul>
		Instrument	Other	<ul style="list-style-type: none"> <li>Rapid fire system (BioTrove)</li> </ul>
	Therapy	Premade	DNA	-
	Environ & Biodefense	Instrument	DNA	<ul style="list-style-type: none"> <li>GeneXpert system (Cepheid)</li> </ul>
			Other	<ul style="list-style-type: none"> <li>Biolzyer (Microfluidic systems)</li> </ul>
Food	Premade	DNA	-	

## BioChip Applications

Type	Applications	Type	Contents	Product Name
Microarray - based	Research	Premade	DNA	<ul style="list-style-type: none"> <li>● GeneChip (Affymetrix), ● Codelink (GE Healthcare), ● Flow-thru chip (Metragenix), ● Agilent Microarray (Agilent), ● Expression Microarray (ABI), ● Sentrix Beadchip (Illumina)</li> </ul>
		Self-made	Protein	<ul style="list-style-type: none"> <li>● Nanochip Electronic microarray (Nanogen)</li> <li>● Protein chip system (CIPHERGEN)</li> <li>● Homebrew protein microarray (Perkin Elmer)</li> </ul>
	Clinical	Premade	DNA	<ul style="list-style-type: none"> <li>● Amplichip CYP450 (Roche)</li> <li>● Influenza A microarray (CombiMatrix)</li> </ul>
		Self-made		<ul style="list-style-type: none"> <li>● Nanochip Electronic microarray (Nanogen)</li> </ul>
		Instrument		<ul style="list-style-type: none"> <li>● GeneChip system 3000 Dx (Affymetrix)</li> </ul>
	Drug Development	Premade	DNA	<ul style="list-style-type: none"> <li>● GeneChip (Affymetrix)</li> <li>● Human toxicity array (Illumina)</li> </ul>
	Therapy	Premade	DNA	<ul style="list-style-type: none"> <li>● Codelink human P450 (GE)</li> <li>● DrugMet Pharmacogenetic test (Nanogen)</li> </ul>
	Environ & Biodefense			-
	Food	Premade	DNA	<ul style="list-style-type: none"> <li>● Food Expert-ID (BioMerieux)</li> </ul>