



UPGRADE YOUR EFFICIENCY

“Industry 4.0” Approach in Pharma Operations:
Continuous Pharmaceutical Production for Oral Solid Dosage
“工业4.0”制药业务方法：口服固体制剂的连续制药生产

Fette Compacting (China) Co. Ltd. 菲特（中国）制药科技有限公司



FETTE
COMPACTING

Agenda

议程

Intro: Industry 4.0 philosophy at a glance 工业4.0观点概述

What is continuous manufacturing in Pharma Production? 在制药行业中，什么是连续性生产？

Advantages and challenges 优点和挑战

Types of continuous manufacturing lines 连续性生产线种类

Continuous wet granulation manufacturing Line 连续性湿法制粒生产线

Direct compression lines 直接压片法生产线

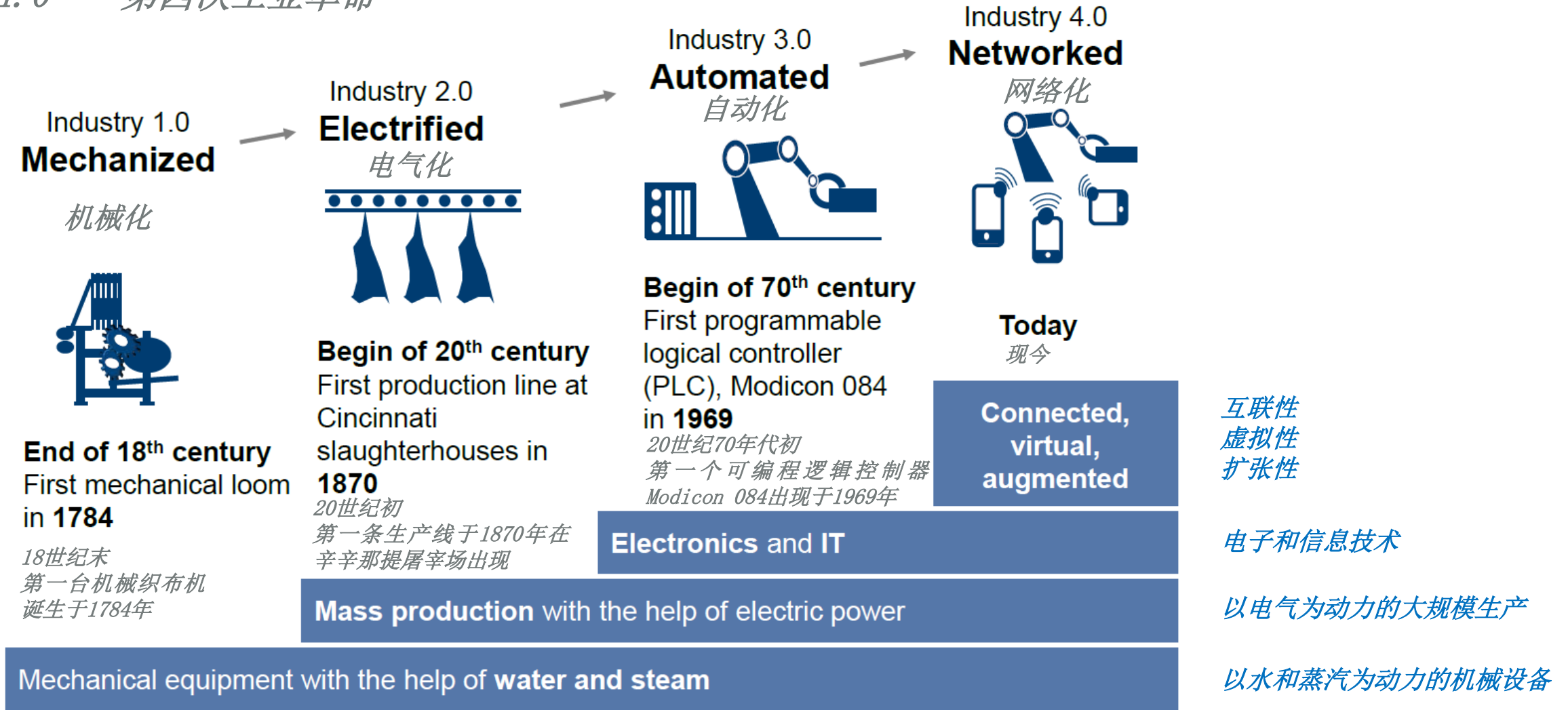
PAT integration PAT整合

• Industry 4.0 – other aspects to be considered

工业4.0 - 其他有待考虑的方面

Industry 4.0 – the 4th Industrial Revolution

工业4.0 - 第四次工业革命

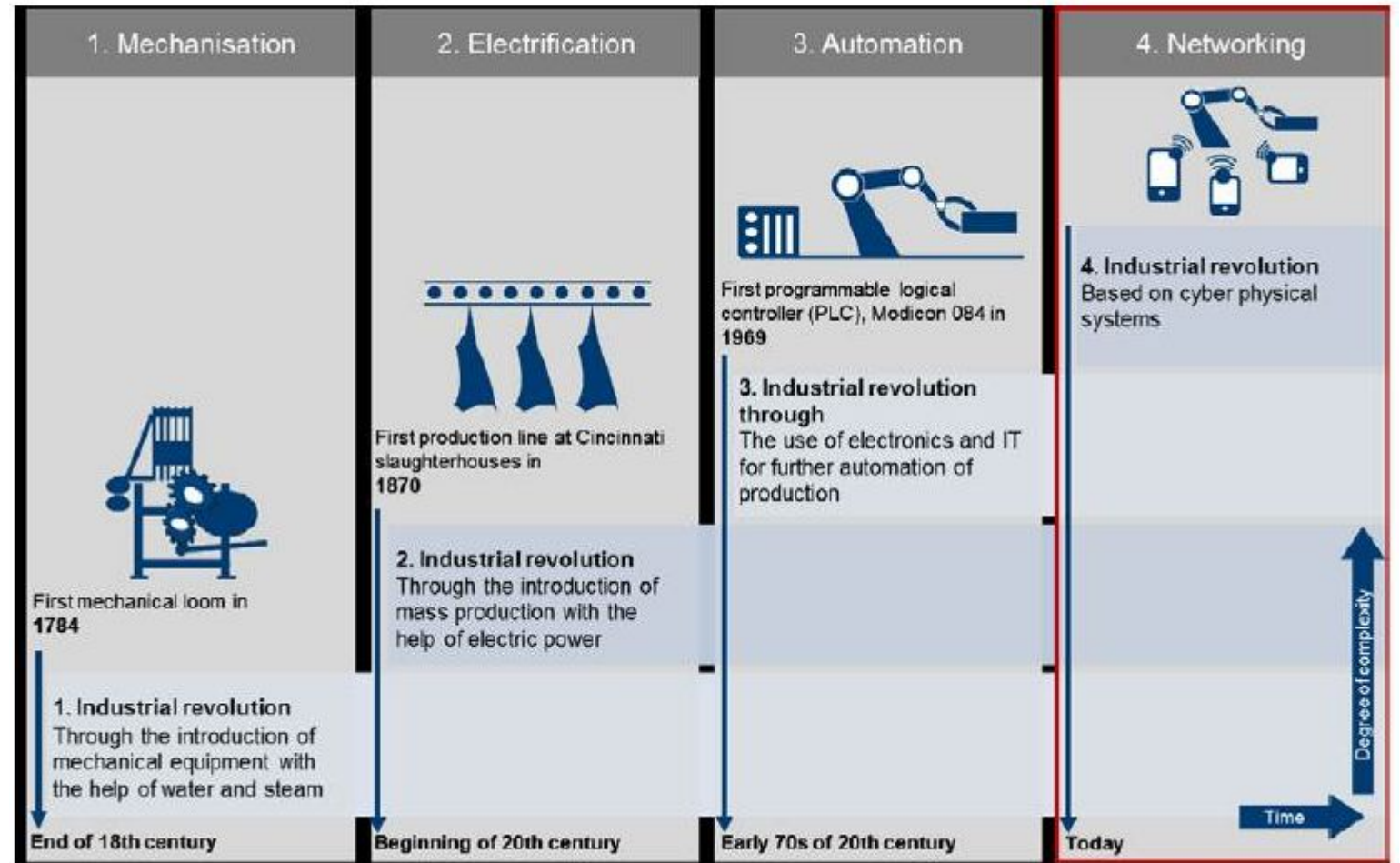


Reference: Umsetzungsempfehlungen für das Zukunftsprojekt Industrie 4.0, April 2013

The Characteristics of Industry 4.0

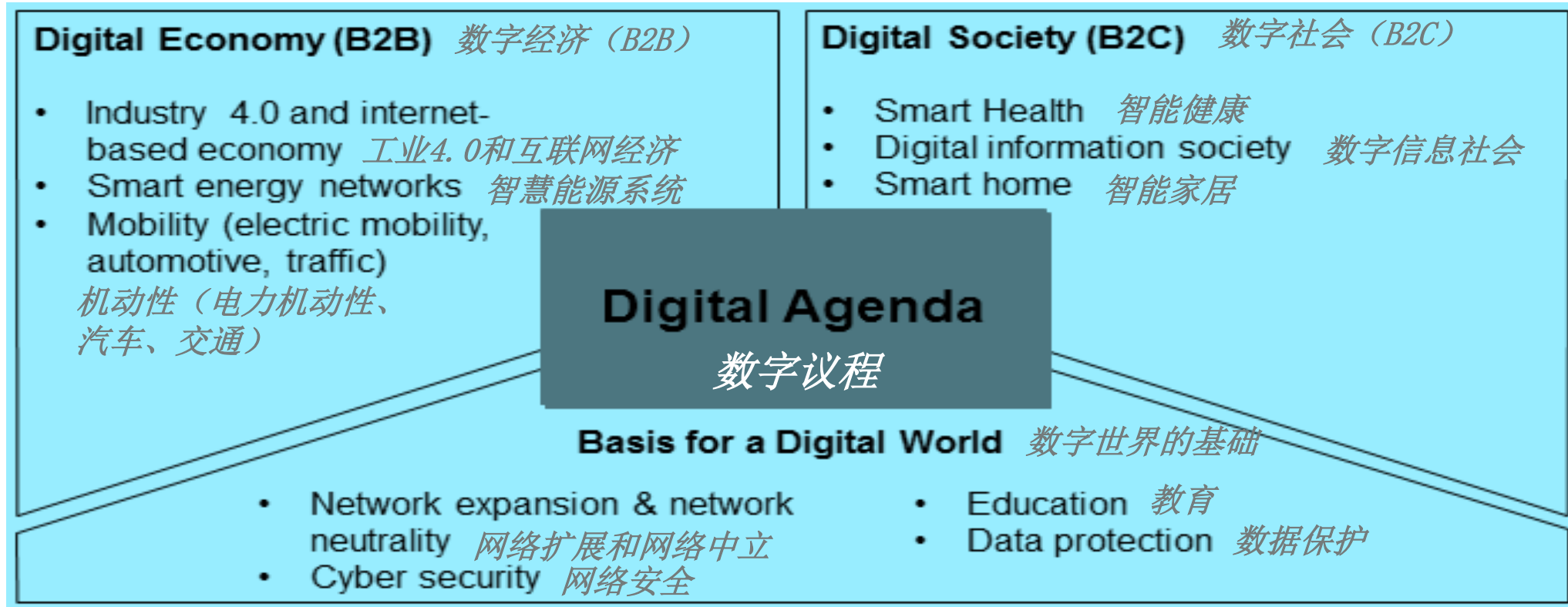
工业4.0的特点

- Goal: Individualization (Lot 1) at the cost of a mass product
全球：以大规模生产为代价的个性化（批量1）
- Highly flexible, productive, resource-efficient production
高度灵活、高生产力、资源节约型生产
- Real-time adjustment and optimization of processes
实时调整和过程优化
- Intelligent assistant systems support the workforce
支持劳动力的智能辅助系统



The Digital Agenda and Industry 4.0 数字议程和工业4.0

1.) The Digital Agenda – not only a production topic 数字议程 - 并非只是生产的课题



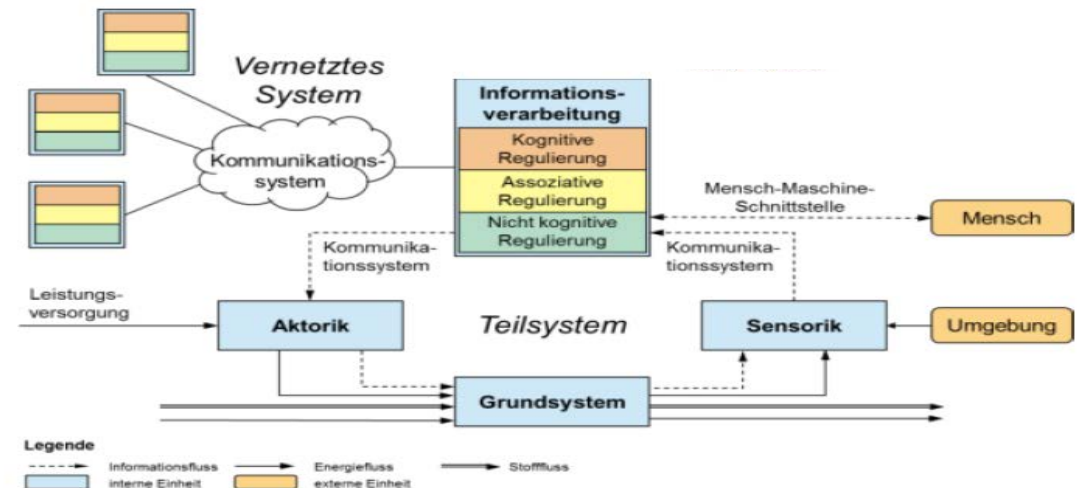
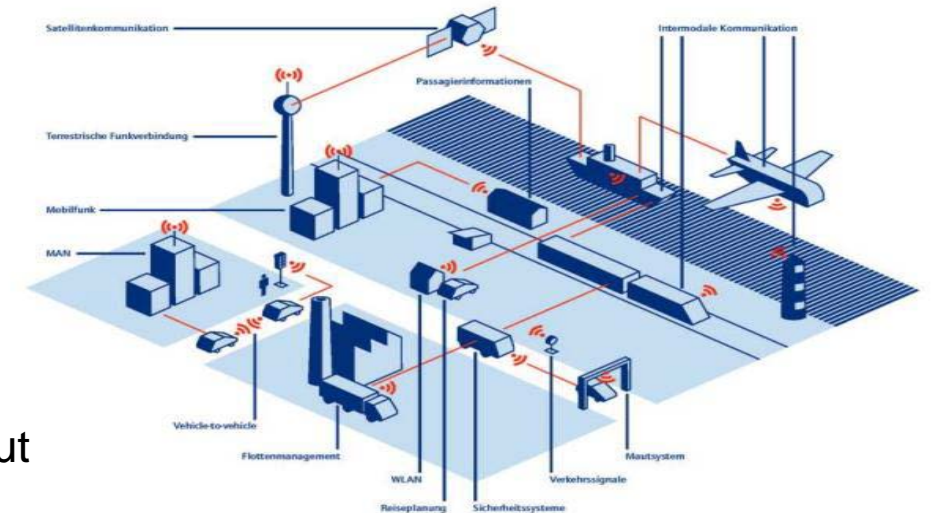
The Digital Agenda and Industry 4.0 数字议程和工业4.0

2.) Industry 4.0

工业4.0

Industry 4.0 – Cyber-Physical Systems 工业4.0 – 网络-物理系统

- Products with embedded hard- and software / Traceability
搭载嵌入式硬件和软件/跟踪的产品
- Sensors and actuators responding to the physical environment / input
响应物理环境/输入的传感器和驱动器
- Use of Internet protocols and services to networking
互联网协议和联网服务的使用
- Interaction across application borders
跨应用程序边界的交互
- Control business and complete value creation networks in real-time
实时列控业务和完整的价值创造网络



Source: www.acatech.de/cps und Gausemeier

The Digital Agenda and Industry 4.0 数字议程和工业4.0

3.) Industry 4.0 – Cyber-physical production systems

Networked people and objects decide cooperatively

3.) 工业4.0 - 网络-物理生产系统 网络化的人和物共同决定

Industry 4.0 and the human being 工业4.0和人类

- Networked objects initiate and deliver information and data for decisions
网络化的对象启动并提供决策所需的信息和数据
- Processing and distribution of information in real-time 实时处理和分发信息
- People / employees do decisions; individually and in groups groups
人员/员工决策; 以个人和团体小组的形式

That means... 这意味着……

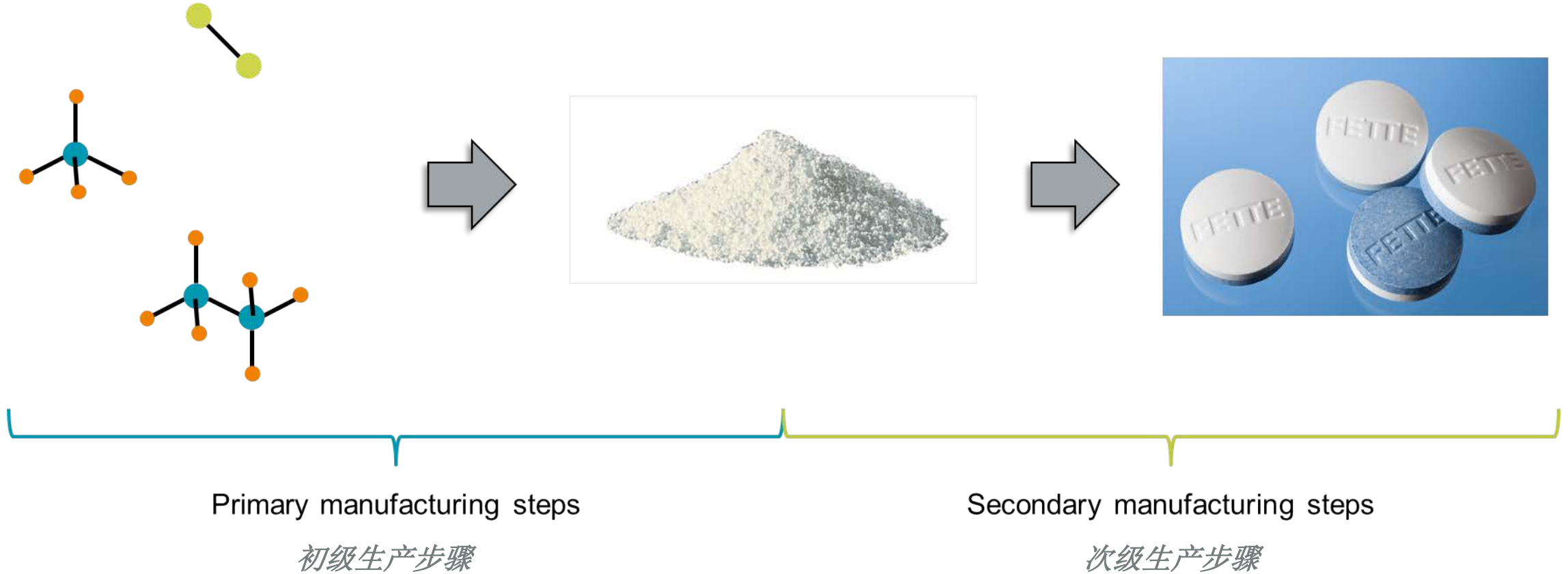
- Mobile information and communication technologies for employees
– even on the shop floor 甚至是车间的员工都可使用移动信息和通信技术
- Access to information in real-time 实时获取信息
- Group communication 团体交流
- **Social Group Decisions** for effective decision findings 社会群体决策产生有效的决策结果

Source: www.acatech.de/cps und Gausemeier



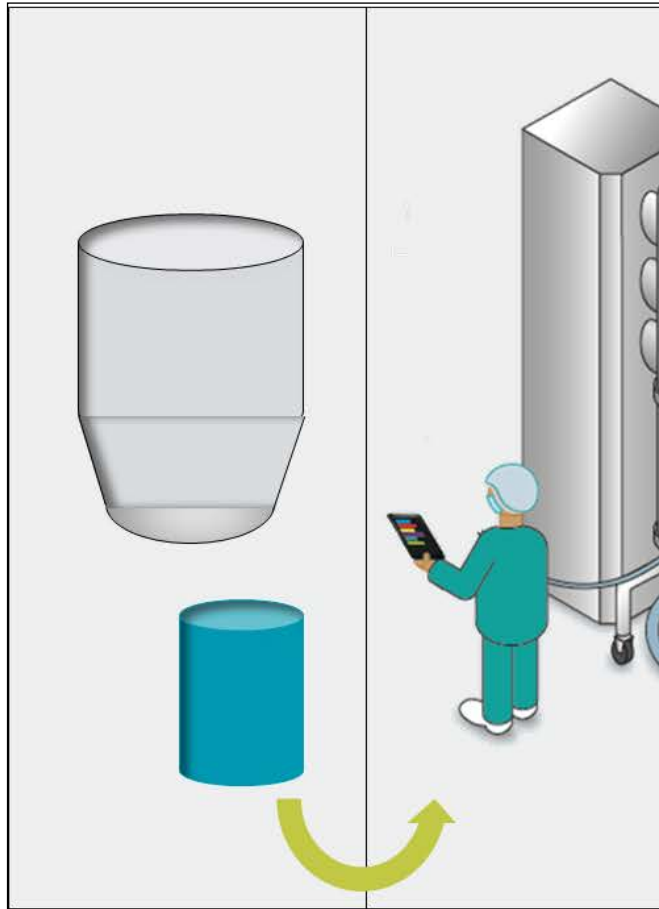
Continuous Pharmaceutical Production

连续性制药生产



Batch vs. Continuous Manufacturing

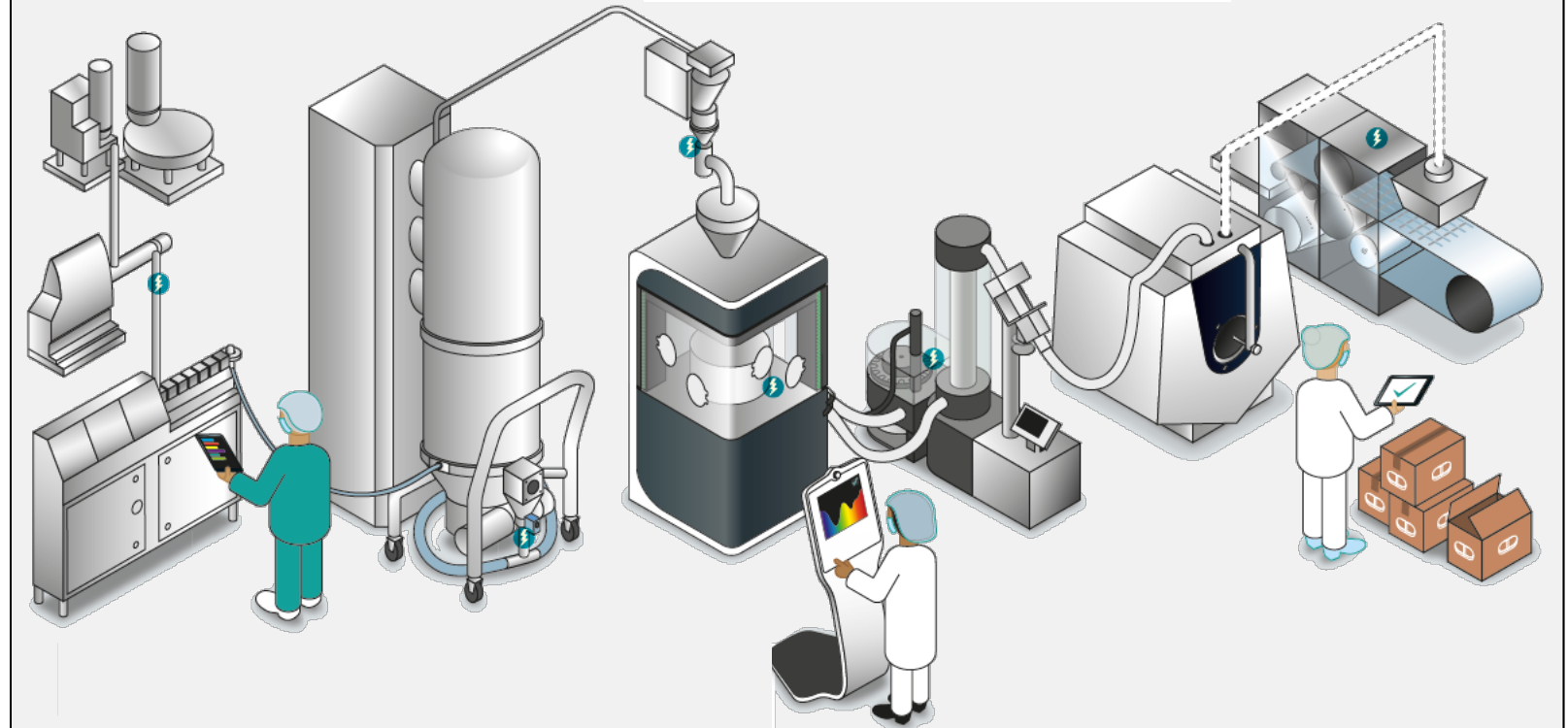
批量生产 vs. 连续性生产



FROM THE DOSER INTO THE BLISTER

A continuous manufacturing scenario for tablet production

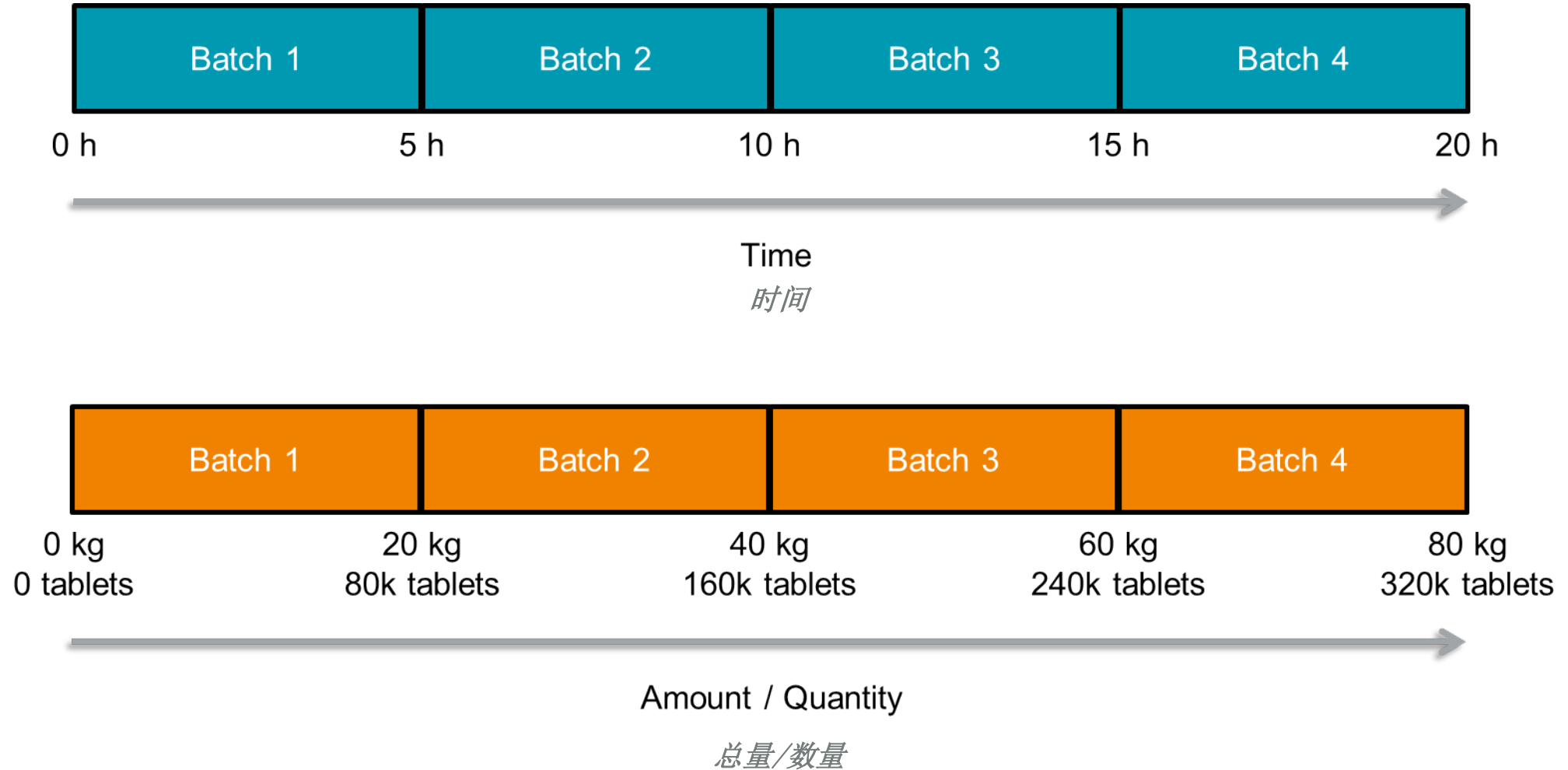
从计量仪进入透明壳
片剂生产的连续性制药场景



Source: Siemens:Continuous manufacturing – Moving towards real-time release

Batch in Continuous Manufacturing

连续性生产中的分批



Motivation & Drivers

动机和驱动力

- Less material handling is required 所需的材料处理更少
- Smaller footprint leads to less energy consumption 占地面积小, 能源消耗低

No intermediate product storage
中间无需存储产品

Safety and Eco Footprint
安全和生态足迹

Lead Time
交货时间

CM to reduce costs
CM可减少成本

CapEx & OpEx
资本支出和运营支出

Time-to-Market
投放时间

Motivation & Drivers

动机和驱动力

Explore a wider range of process parameters with less material and in less time 以 fewer 的材料和更少的时间探索更广泛的工艺参数

Batch Size
批量大小

Possibility of producing virtually any required batch size with smaller equipment range
可以在较小的设备范围内生产几乎所有需要的批量

Scale-Up
可按比例增加

Flexible batch size determined by time and production capacity
可由时间和生产能力灵活决定批量大小

Product Loss and QA Costs
产品损耗和质量保证成本

Process performance	Yield
2-sigma	69.2%
3-sigma	93.3%
4-sigma	99.4%
5-sigma	99.98%
6-sigma	99.99966%

Product Quality
产品质量

Implementation of PAT and APC to achieve higher process stability 采用PAT和APC, 获得更高的工艺稳定性

Technical challenges

技术挑战

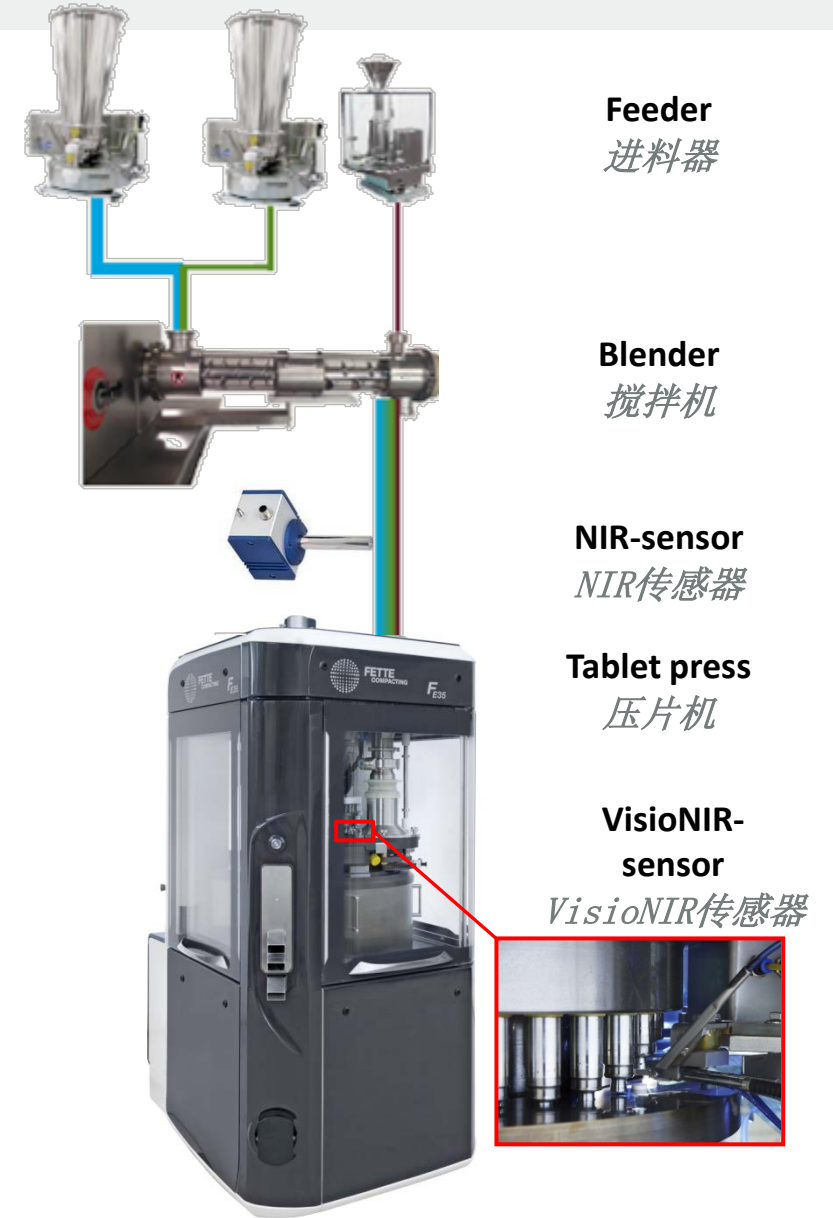


Continuous Manufacturing - Key Facts 连续性生产 - 重要事实

- 1 Big Pharma has widely evaluated CM in the last 5 to 10 years.**
在过去的5到10年中，大型制药公司广泛评估了CM。
 - ▶ The point-of-no-return has been crossed!
- 2 Generic manufacturers are behind Big Pharma but currently start to invest.**
一般厂家落后于大型制药公司，但现在也已开始投资。
- 3 Wet Granulation and Direct Compression are both important.** *湿法制粒和直接压片都很重要。*
 - ▶ Wet Granulation (WG) is at the moment the dominant route of manufacturing
 - ▶ Direct Compression (DC) is often selected for first investment in CM as it is simpler than WG
- 4 CM is relevant for new drugs and also existing batch products!** *CM与新药和现有批次产品紧密相关!*
 - ▶ Vertex got FDA approval for a new drug Orakambi
 - ▶ J&J got first FDA approval for shift from batch to CM for Prezista in early 2016
- 5 CM is promoted by FDA.** *FDA在推广CM。*
- 6 Equipment suppliers have started to develop CM technologies and equipment:**
Fette Compacting, Glatt, GEA, Bohle, Bosch,
设备供应商已经开始开发CM技术和设备: GEA, Glatt, Bohle, Bosch Fette Compacting.

Test Facility at Fette Compacting Germany

德国菲特测试设备



Technical Aspects of the Tablet Press

压片机技术现状



Industry 4.0 implementation

The major challenges are still in the field of IT

工业4.0实施 IT领域仍存在重大挑战

Unique identification 唯一标识

- > IPv4 addresses are used up (4.3 bil.)
- > IPv6 is hardly applied by corporations
- > IPv6 is essential for the "Internet of Things"

Basis for
Internet of Things

物联网基础

Intercommunication 交互性

- > many protocols available
- > no standard protocol determined
- > industry-specific solutions on the way
- > Combination of IT security and operational safety

Basis for
Industry 4.0

工业4.0基础

IT security and trust 信息安全信任

- > Access control → available, applied
- > Usage control → available, hesitation of industry

Basis for
Digital Factories /
Additive Manufacturing

数字化工厂/
附加加工基础

Industry 4.0 is more than just Technology ... it is a holistic concept

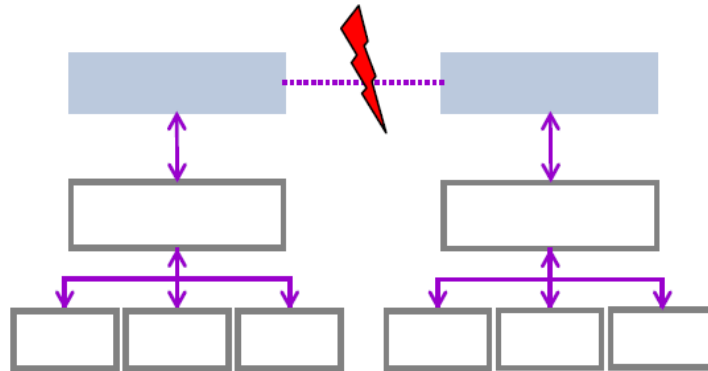
工业4.0不仅只是技术，更是一种整体观念

现在的信息使用

- 间接信息流，互不关联
- 极少记录数据，常手动转换数据
- 无/低效使用现有数据
- 工业领域很少使用“分析学”

Information usage today

- Indirect information flow, non-connected
- Few data is recorded, often converted manually
- No / inefficient usage of available data
- Few usage of “Analytics” in the industry sector



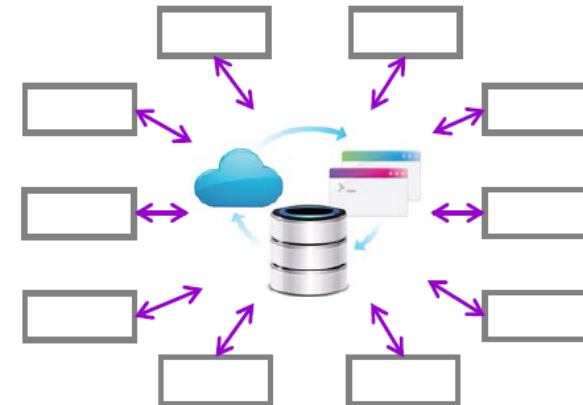
→ information flow

Information usage tomorrow

- Direct information flow
- Central high-scale collection and processing of heterogeneous data
- Digital copies of machines and factories
- “Big Data”, “Analytics”, and simulations
 - > Real time monitoring and predictions
 - > Maintenance and reliability forecasts
 - > New after-sales services

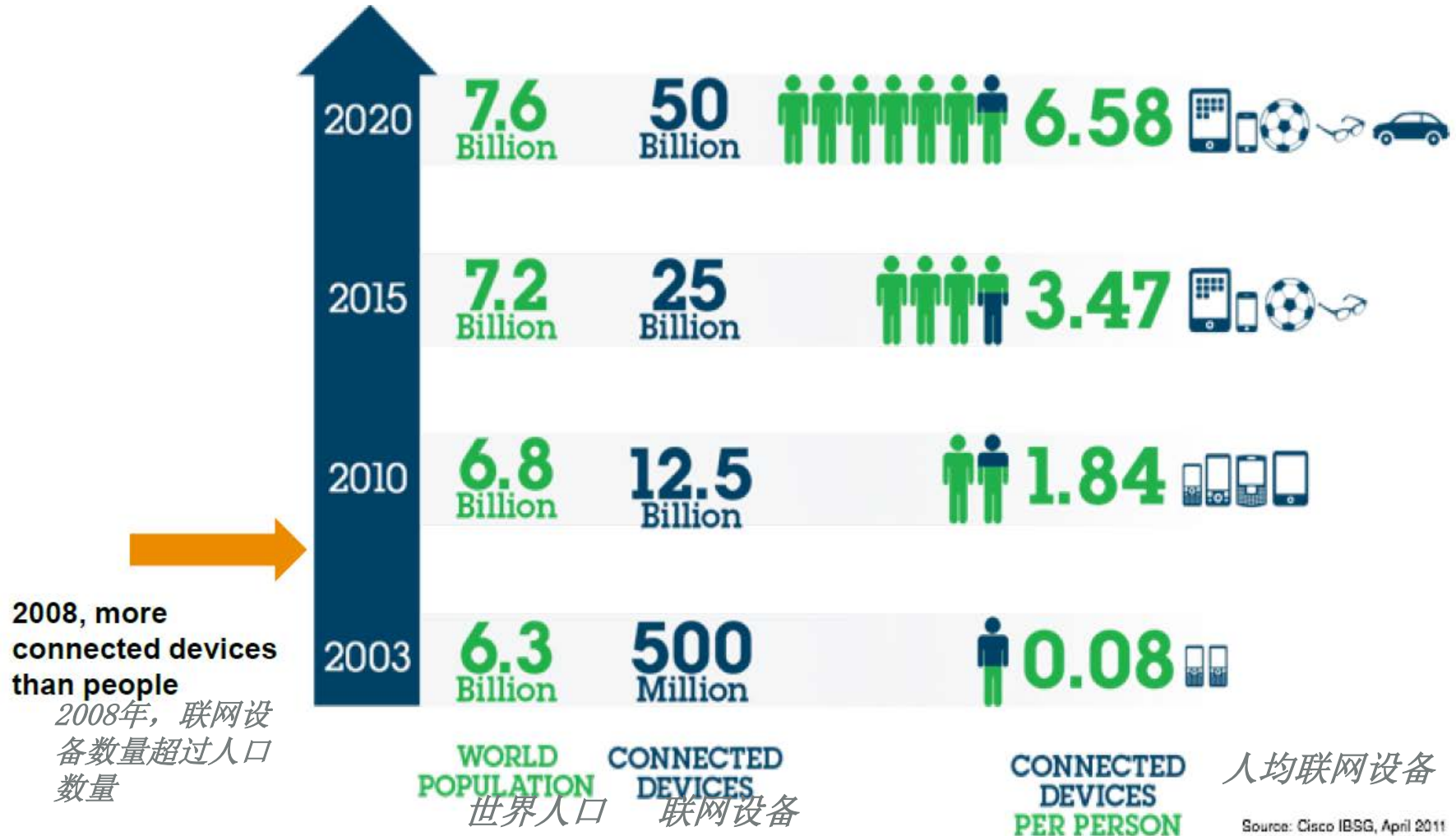
未来的信息使用

- 直接信息流
- 大规模集中收集、处理异构数据
- 机器和工厂的数字副本
- “大数据”、“分析学”和模拟
 - > 实时监控和预测
 - > 维护和可靠性预测
 - > 新型售后服务



Connected Devices exceed the world population ... already since 2008

2008年起联网设备已超过世界人口



Successful implementation of Industry 4.0 requires to address and overcome challenges

成功实施工业4.0需要克服各种挑战

Human aspects 人员方面

- > Employees' acceptance of the new technology
- > Qualification and Training
- > Motivation and continuous learning

IT and legal aspects 信息技术和法律方面

- > Hesitation towards changing a running system
- > Hesitation towards transparency among the supply chain
- > Slow establishment of norms and standards

Exotic products 国外产品

- > The whole supply chain / manufacturing process needs to be pre-planned and digitalized
→ potential effort / output gap

Data quantity and quality 数据数量和质量

- > Limited real-time processing capability
- > Selective data processing
- > Users' resistance towards continuous machine monitoring and analytics by the manufacturer

Organizational aspects 组织方面

- > From "central planning" to "decentralized control"
- > Changing processes and functions
- > Cooperation with workers councils

A real paradigm shift:

"Industry 4.0" cannot be realized with Users & Operators on "level 2.0 / 3.0"

真正的范式转变:

"2.0/3.0的用户和经营者无法实现工业4.0"

THANK YOU!